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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 12	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 13	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 15	AUG 27	USPATOLD now available on STN
NEWS 16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 18	SEP 13	FORIS renamed to SOFIS
NEWS 19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 20	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 23	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 24	OCT 19	BEILSTEIN updated with new compounds

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:47:08 ON 13 NOV 2007

=> file reg
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                         ENTRY   SESSION
FULL ESTIMATED COST   0.21   0.21

FILE 'REGISTRY' ENTERED AT 13:47:17 ON 13 NOV 2007

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 12 NOV 2007 HIGHEST RN 953132-99-5
DICTIONARY FILE UPDATES: 12 NOV 2007 HIGHEST RN 953132-99-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s 1,2-di(cyclic)substituted benzene compounds
MISSING OPERATOR '1,2-DI(CYCLIC'

=> s 1,2-di
=> s 1,2-di!
       1310613 1,2
        501230 DI!
L1   5 1,2-DI!
                 (1,2(W)DI!)

=> s l1 and autoimmune disease
            94 AUTOIMMUNE
        269203 DISEASE
             2 DISEASES
        269203 DISEASE
                 (DISEASE OR DISEASES)
            78 AUTOIMMUNE DISEASE
                 (AUTOIMMUNE(W)DISEASE)
L2   0 L1 AND AUTOIMMUNE DISEASE

```
=> s (cell adhesion inhibitor or cell infiltration inhibitor)
        658848 CELL
         22848 CELLS
        659439 CELL
                  (CELL OR CELLS)
          3715 ADHESION
         15733 INHIBITOR
            30 INHIBITORS
         15760 INHIBITOR
                  (INHIBITOR OR INHIBITORS)
             0 CELL ADHESION INHIBITOR
                  (CELL(W)ADHESION(W)INHIBITOR)
        658848 CELL
         22848 CELLS
        659439 CELL
                  (CELL OR CELLS)
             1 INFILTRATION
         15733 INHIBITOR
            30 INHIBITORS
         15760 INHIBITOR
                  (INHIBITOR OR INHIBITORS)
             0 CELL INFILTRATION INHIBITOR
                  (CELL(W)INFILTRATION(W)INHIBITOR)
L3           0 (CELL ADHESION INHIBITOR OR CELL INFILTRATION INHIBITOR)

=> s cell adhesion inhibitor
        658848 CELL
         22848 CELLS
        659439 CELL
                  (CELL OR CELLS)
          3715 ADHESION
         15733 INHIBITOR
            30 INHIBITORS
         15760 INHIBITOR
                  (INHIBITOR OR INHIBITORS)
L4           0 CELL ADHESION INHIBITOR
                  (CELL(W)ADHESION(W)INHIBITOR)

=> file medlinme
'MEDLINME' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'REGISTRY'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.

=> file medline
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  74.25      74.46

FILE 'MEDLINE' ENTERED AT 14:00:14 ON 13 NOV 2007

 FILE LAST UPDATED: 10 Nov 2007 (20071110/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s (cell adhesion inhibitor or cell infiltration inhibitor)
       2190278 CELL
```

```
       1978654 CELLS
       2907941 CELL
                 (CELL OR CELLS)
        127046 ADHESION
         17038 ADHESIONS
        139021 ADHESION
                 (ADHESION OR ADHESIONS)
        308099 INHIBITOR
        622041 INHIBITORS
        761192 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
            22 CELL ADHESION INHIBITOR
                 (CELL(W)ADHESION(W)INHIBITOR)
       2190278 CELL
       1978654 CELLS
       2907941 CELL
                 (CELL OR CELLS)
         54393 INFILTRATION
          2527 INFILTRATIONS
         56396 INFILTRATION
                 (INFILTRATION OR INFILTRATIONS)
        308099 INHIBITOR
        622041 INHIBITORS
        761192 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
             2 CELL INFILTRATION INHIBITOR
                 (CELL(W)INFILTRATION(W)INHIBITOR)
L5           24 (CELL ADHESION INHIBITOR OR CELL INFILTRATION INHIBITOR)

=> s l5 and autoimmune disease
         84744 AUTOIMMUNE
            43 AUTOIMMUNES
         84744 AUTOIMMUNE
                 (AUTOIMMUNE OR AUTOIMMUNES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                 (DISEASE OR DISEASES)
         48478 AUTOIMMUNE DISEASE
                 (AUTOIMMUNE(W)DISEASE)
L6            0 L5 AND AUTOIMMUNE DISEASE

=> s 1,2-di!
       4120520 1
       3632022 2
       1132561 DI!
L7           77 1,2-DI!
                 (1(W)2(W)DI!)

=> s l7 and autoimmune disease
         84744 AUTOIMMUNE
            43 AUTOIMMUNES
         84744 AUTOIMMUNE
                 (AUTOIMMUNE OR AUTOIMMUNES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                 (DISEASE OR DISEASES)
         48478 AUTOIMMUNE DISEASE
                 (AUTOIMMUNE(W)DISEASE)
```

```
L8            0 L7 AND AUTOIMMUNE DISEASE

=> s autoimmune disease
          84744 AUTOIMMUNE
             43 AUTOIMMUNES
          84744 AUTOIMMUNE
                (AUTOIMMUNE OR AUTOIMMUNES)
        1952243 DISEASE
        1748322 DISEASES
        3226949 DISEASE
                (DISEASE OR DISEASES)
L9        48478 AUTOIMMUNE DISEASE
                (AUTOIMMUNE(W)DISEASE)

=> s l9 and dopaminergic agent
          29935 DOPAMINERGIC
             21 DOPAMINERGICS
          29946 DOPAMINERGIC
                (DOPAMINERGIC OR DOPAMINERGICS)
         203048 AGENT
        1214842 AGENTS
        1339626 AGENT
                (AGENT OR AGENTS)
            588 DOPAMINERGIC AGENT
                (DOPAMINERGIC(W)AGENT)
L10           1 L9 AND DOPAMINERGIC AGENT

=> d ibib abs hitstr tot
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'MEDLINE'

The following are valid formats:

The default display format is BIB.

ABS ---- AB
ALL ---- AN, DN, TI, AU, CS, NC, SO, CM, CY, DT, LA, FS, NCT, OS,
         EM, ED, AB, ST, CT, NA, RN, CN, GEN
BIB ---- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
CBIB --- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
DALL --- ALL, delimited for post processing
IABS --- ABS, with a text label
IALL --- ALL, indented with text labels
IBIB --- BIB, indented with text labels
IND ---- ST, CT, NA, RN, CN, GEN
TRIAL -- TI, ST, CT, NA, RN, CN, GEN
 (SAM, TRI, FREE)
HIT ---- All fields containing hit terms
HITIND - IND
KWIC --- All hit terms plus 20 words on either side
OCC ---- List of display fields containing hit terms

Hit terms will be highlighted in all available fields except CM and
PY.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,ST'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.
```

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.
ENTER DISPLAY FORMAT (BIB):d l10 full
'D' IS NOT A VALID FORMAT FOR FILE 'MEDLINE'

The following are valid formats:

The default display format is BIB.

ABS ---- AB
ALL ---- AN, DN, TI, AU, CS, NC, SO, CM, CY, DT, LA, FS, NCT, OS,
EM, ED, AB, ST, CT, NA, RN, CN, GEN
BIB ---- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
CBIB --- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
DALL --- ALL, delimited for post processing
IABS --- ABS, with a text label
IALL --- ALL, indented with text labels
IBIB --- BIB, indented with text labels
IND ---- ST, CT, NA, RN, CN, GEN
TRIAL -- TI, ST, CT, NA, RN, CN, GEN
(SAM, TRI, FREE)
HIT ---- All fields containing hit terms
HITIND - IND
KWIC --- All hit terms plus 20 words on either side
OCC ---- List of display fields containing hit terms

Hit terms will be highlighted in all available fields except CM and
PY.

To display a particular field or fields, enter the display field
codes. For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>). Examples of formats include: 'BIB';
'AB'; 'SO,ST'. You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.
ENTER DISPLAY FORMAT (BIB):.

L10 ANSWER 1 OF 1 MEDLINE on STN
AN 94082608 MEDLINE Full-text
DN PubMed ID: 8259781
TI Prolactin and immunomodulation.
AU Reber P M
CS Department of Internal Medicine, University of Wisconsin Medical School,
Madison.
SO The American journal of medicine, (1993 Dec) Vol. 95, No. 6, pp. 637-44.
Ref: 64
Journal code: 0267200. ISSN: 0002-9343.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199401
ED Entered STN: 3 Feb 1994

```
     Last Updated on STN: 3 Feb 1994
     Entered Medline: 19 Jan 1994


=> FIL STNGUIDE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.12      76.58

FILE 'STNGUIDE' ENTERED AT 14:03:23 ON 13 NOV 2007
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Nov  9, 2007 (20071109/UP).

=> s ABT-724
             0 ABT
             0 724
L11          0 ABT-724
                   (ABT(W)724)

=> s dopamin!
L12          0 DOPAMIN!

=> s dopamin
=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.36      76.94

FILE 'MEDLINE' ENTERED AT 14:07:16 ON 13 NOV 2007

 FILE LAST UPDATED: 10 Nov 2007 (20071110/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s dopamin!
L13     100180 DOPAMIN!

=> s l13 and autoimmune disease
          84744 AUTOIMMUNE
             43 AUTOIMMUNES
          84744 AUTOIMMUNE
                   (AUTOIMMUNE OR AUTOIMMUNES)
        1952243 DISEASE
        1748322 DISEASES
        3226949 DISEASE
                   (DISEASE OR DISEASES)
          48478 AUTOIMMUNE DISEASE
                   (AUTOIMMUNE(W)DISEASE)
L14          51 L13 AND AUTOIMMUNE DISEASE

=> s l14 and py>2002
        3057410 PY>2002
                   (PY>20029999)
L15          14 L14 AND PY>2002

=> d ibib abs tot
```

L15 ANSWER 1 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2007538804 IN-PROCESS Full-text
DOCUMENT NUMBER: PubMed ID: 17854745
TITLE: Hyperprolactinemia and autoimmune diseases.
AUTHOR: Orbach Hedi; Shoenfeld Yehuda
CORPORATE SOURCE: Department of Medicine B, Wolfson Medical Center, Holon, Israel.
SOURCE: Autoimmunity reviews, (2007 Sep) Vol. 6, No. 8, pp. 537-42. Electronic Publication: 2006-12-01. Journal code: 101128967. ISSN: 1568-9972.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 15 Sep 2007
Last Updated on STN: 24 Oct 2007

AB The autoimmune diseases are more common in females. The sex hormones have an important role in this gender bias, mainly estrogen and prolactin (PRL) which modulate the immune response. PRL is secreted from the pituitary gland and other organs and cells mainly the lymphocytes. PRL has an immunostimulatory effect and promotes autoimmunity: PRL impairs the negative selection of autoreactive B lymphocytes occurring during B cell maturation into fully functional B cells. PRL has an anti-apoptotic effect, enhances proliferative response to antigens and mitogens and enhances the production of immunoglobulins and autoantibodies. Hyperprolactinemia (HPRL) is observed in multi-organ and organ specific autoimmune diseases like systemic lupus erythematosus (SLE) rheumatoid arthritis (RA), Sjogren's syndrome (SS), Hashimoto's thyroiditis (HT) and multiple sclerosis (MS). There is no consistent correlation between PRL levels and disease activity. Murine models and small studies in SLE patients suggest some role of dopamine agonists in the therapy of those diseases. The genetic factor may have a role in humans as in animal models. The PRL isoform has an important effect on the bioactivity on prolactin receptors (PRL-Rs).

L15 ANSWER 2 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2007519321 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17785327
TITLE: Novel biomarkers in autoimmune diseases : prolactin, ferritin, vitamin D, and TPA levels in autoimmune diseases.
AUTHOR: Orbach Hedi; Zandman-Goddard Gisele; Amital Howard; Barak Vivian; Szekanecz Zoltan; Szucs Gabriella; Danko Katalin; Nagy Endre; Csepany Tunde; Carvalho Jozelio F; Doria Andrea; Shoenfeld Yehuda
CORPORATE SOURCE: Department of Medicine B, Wolfson Medical Center, Holon, Israel.. orbach@wolfson.health.gov.il
SOURCE: Annals of the New York Academy of Sciences, (2007 Aug) Vol. 1109, pp. 385-400. Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200710
ENTRY DATE: Entered STN: 6 Sep 2007
Last Updated on STN: 3 Oct 2007
Entered Medline: 2 Oct 2007

AB The development of autoimmune diseases may be influenced by hormonal, immunomodulatory, and metabolic pathways. Prolactin (PRL), ferritin, vitamin D, and the tumor marker tissue polypeptide antigen (TPA) were measured in autoimmune diseases: systemic lupus erythematosus (SLE), systemic sclerosis (SSc), rheumatoid arthritis (RA), polymyositis (PM), dermatomyositis (DM), multiple sclerosis (MS), autoimmune thyroid diseases, and antiphospholipid syndrome. Hyperprolactinemia (HPRL) was detected in 24% of PM patients, in 21% of SLE patients, in 6.7% of MS patients, 6% of RA patients, and in 3% of SSc patients. Hyperferritinemia was detected in 23% of SLE patients, 15% of DM patients, 8% of MS patients, and 4% of RA patients. The patients had relatively low levels of 25 OH Vitamin D: the average results (mean +/- SD) were between 9.3 +/- 4.4 to 13.7 +/- 7.1 ng/mL in the different diseases, while the 25 OH Vitamin D concentrations less than 20 ng/mL are regarded as deficient. TPA levels were in the same range of the controls, elevated only in SLE. HPRL, hyperferritinemia, hypovitaminosis D, and TPA levels did not correlate with SLE activity elevated levels of rheumatoid factor or anti-CCP antibodies in RA. HPRL, hyperferritinemia, and hypovitaminosis D have different immunological implications in the pathogenesis of the autoimmune diseases. Preventive treatment with vitamin D or therapy for HPRL with dopamine agonists, may be considered in certain cases. Hyperferritinemia may be used as an acute-phase reactant marker in autoimmune diseases mainly SLE. TPA may be used to indicate the tendency for malignancies.

L15 ANSWER 3 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2007469019 IN-PROCESS Full-text
DOCUMENT NUMBER: PubMed ID: 17687515
TITLE: MPTP-induced central dopamine depletion exacerbates experimental autoimmune encephalomyelitis (EAE) in C57BL mice.
AUTHOR: Balkowiec-Iskra E; Kurkowska-Jastrzebska I; Joniec I; Ciesielska A; Muszynska A; Przybylkowski A; Czlonkowska A; Czlonkowski A
CORPORATE SOURCE: Department of Experimental and Clinical Pharmacology, The Medical University of Warsaw, Krakowskie Przedmiescie 26/28, 00-927, Warsaw, Poland,. ewazbi@amwaw.edu.pl
SOURCE: Inflammation research : official journal of the European Histamine Research Society ... [et al.], (2007 Aug) Vol. 56, No. 8, pp. 311-7.
Journal code: 9508160. ISSN: 1023-3830.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 10 Aug 2007
Last Updated on STN: 10 Aug 2007

AB It is obvious that the central nervous system plays a role in the regulation of an immune response. However, the mechanisms of this regulation are poorly understood. The goal of the present study was to examine the role of one of the neurotransmitters - dopamine, in this process. We used experimental autoimmune encephalomyelitis (EAE), an autoimmune disease with its effector phase in the CNS, as a model to study the effect of central dopamine depletion on the development of an immune response. Dopamine depletion was achieved by treatment with 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropiridine (MPTP; 40 mg/kg), whereas EAE was elicited by immunization with MOG 35-55 (150 mug) in complete Freund's adjuvant (CFA), supplemented with Mycobacterium tuberculosis. As determined by HPLC, striatal dopamine contents in mice treated with MPTP were significantly lower compared to vehicle-treated controls. Remarkably, striatal depletion of dopamine prior to EAE induction

resulted in an earlier onset of the disease and an augmentation of its clinical signs. Moreover, the striatal dopamine-depleted mice demonstrated an increased concentration of IL-1beta and decreased concentration of TGFbeta in the spinal cord, compared to EAE mice. Since MPTP itself does not have any direct effect on immune cells, it strongly suggests that the observed changes in EAE induction and progression after MPTP administration depended on lower dopamine level. Further studies are required to find out the cellular mechanism of the dopamine action.

L15 ANSWER 4 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2007257919 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17465339
TITLE: Prolactin and autoimmune diseases in humans.
AUTHOR: Chuang Ellie; Molitch Mark E
CORPORATE SOURCE: Division of Endocrinology, Metabolism and Molecular Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois 60611, USA.
SOURCE: Acta bio-medica : Atenei Parmensis, (2007) Vol. 78 Suppl 1, pp. 255-61.
Journal code: 101295064. ISSN: 0392-4203.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (LECTURES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200706
ENTRY DATE: Entered STN: 1 May 2007
Last Updated on STN: 30 Jun 2007
Entered Medline: 29 Jun 2007

AB Prolactin has been shown to have immunomodulatory as well as lactogenic effects. Generally less well known is that prolactin may also play a role in the activity of autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis. Studies have shown decreasing prolactin production to be beneficial in animal models of autoimmune disease. Thus far, double-blinded, placebo-controlled studies of dopamine agonist treatment in humans with autoimmune disease have been done only in lupus patients, and support the potential efficacy of such agents. Small, open-label trials have also suggested potential benefit in patients with rheumatoid arthritis, Reiter's syndrome, and psoriasis. More studies are required to further delineate the mechanisms by which prolactin affects autoimmune disease activity, to determine in which specific diseases prolactin plays a significant role, and to test the efficacy of prolactin-lowering agents as therapy for such diseases.

L15 ANSWER 5 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2007251494 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17223198
TITLE: Neuroimmunopathology in a murine model of neuropsychiatric lupus.
AUTHOR: Ballok David A
CORPORATE SOURCE: Department of Psychiatry and Behavioral Neurosciences, HSC Rm 4N4, McMaster University, 1200 Main St. West, Hamilton, Ontario, Canada L8N 3Z5.. ballokda@mcmaster.ca
SOURCE: Brain research reviews, (2007 Apr) Vol. 54, No. 1, pp. 67-79. Electronic Publication: 2006-12-20. Ref: 162
Journal code: 101300366. ISSN: 0165-0173.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200706
ENTRY DATE: Entered STN: 28 Apr 2007
Last Updated on STN: 22 Jun 2007
Entered Medline: 21 Jun 2007

AB Animal models are extremely useful tools in defining pathogenesis and treatment of human disease. For many years researchers believed that structural damage to the brain of neuropsychiatric (NP) patients lead to abnormal mental function, but this possibility was not extensively explored until recently. Imaging studies of NP-systemic lupus erythematosus (SLE) support the notion that brain cell death accounts for the emergence of neurologic and psychiatric symptoms, and evidence suggests that it is an autoimmunity-induced brain disorder characterized by profound metabolic alterations and progressive neuronal loss. While there are a number of murine models of SLE, this article reviews recent literature on the immunological connections to neurodegeneration and behavioral dysfunction in the Fas-deficient MRL model of NP-SLE. Probable links between spontaneous peripheral immune activation, the subsequent central autoimmune/inflammatory responses in MRL/MpJ-Tnfrsf6(lpr) (MRL-lpr) mice and the sequential mode of events leading to Fas-independent neurodegenerative autoimmune-induced encephalitis will be reviewed. The role of hormones, alternative mechanisms of cell death, the impact of central dopaminergic degeneration on behavior, and germinal layer lesions on developmental/regenerative capacity of MRL-lpr brains will also be explored. This model can provide direction for future therapeutic interventions in patients with this complex neuroimmunological syndrome.

L15 ANSWER 6 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2006481897 IN-PROCESS Full-text
DOCUMENT NUMBER: PubMed ID: 16906330
TITLE: Immunoregulatory role of endogenous catecholamines synthesized by immune cells.
AUTHOR: Jiang Jian-Lan; Qiu Yi-Hua; Peng Yu-Ping; Wang Jian-Jun
CORPORATE SOURCE: Department of Biological Science and Technology, School of Life Sciences, Nanjing University, Nanjing 210093, China; Department of Physiology, School of Basic Medical Sciences, Nantong University, Nantong 226001, China. E-mail:. yppeng@ntu.edu.cn
SOURCE: Sheng li xue bao : [Acta physiologica Sinica], (2006 Aug 25) Vol. 58, No. 4, pp. 309-17.
Journal code: 20730130R. ISSN: 0371-0874.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 15 Aug 2006
Last Updated on STN: 12 Dec 2006

AB It has been well known that catecholamines (CAs) in the body, including norepinephrine (NE), epinephrine (E) and dopamine (DA), are synthesized and secreted by neurons and endocrine cells and mainly modulate visceral activities such as cardiovascular, respiratory and digestive functions. The studies over the past nearly 30 years have shown that CAs can also regulate immune function. The immunomodulation of CAs is generally considered as a role mediating the regulation of nervous and endocrine systems. However, recent studies reveal that immune cells can also synthesize CAs, which is an update of traditional concept. A classical metabolic pathway of CAs shared by

the nervous and endocrine systems is present in the immune cells, i.e., the immunocytes have the enzymes for synthesis of CAs [e.g. tyrosine hydroxylase (TH)] and the enzymes for degradation of CAs [e.g. monoamine oxidase (MAO) and catechol-O-methyl transferase (COMT)]. The endogenous CAs synthesized by immune cells can regulate many immune functions, including cellular proliferation, differentiation, apoptosis and cytokine production. These roles of the endogenous CAs may be mediated by an autocrine/paracrine pathway via relevant receptors on the immunocytes and intracellular cAMP. Intracellular oxidative mechanism may also be involved in immunoregulation of endogenous CAs in immune cells. In addition, some metabolic abnormalities of CAs in the immune cells probably induce some autoimmune diseases, such as multiple sclerosis (MS) and rheumatoid arthritis. These findings not only provide evidence for the new concept that the immune system is possible to become the third CA system other than the nervous and endocrine systems, but also extend our comprehension on functional significance of the endogenous CAs synthesized by immune cells.

L15 ANSWER 7 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2006421164 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16842192
TITLE: Catecholamines: physiological immunomodulators during health and illness.
AUTHOR: Oberbeck Reiner
CORPORATE SOURCE: Dept. Trauma Surgery, University Hospital of Essen, Essen Germany.. reineroberbeck@hotmail.com
SOURCE: Current medicinal chemistry, (2006) Vol. 13, No. 17, pp. 1979-89. Ref: 201
Journal code: 9440157. ISSN: 0929-8673.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200607
ENTRY DATE: Entered STN: 18 Jul 2006
Last Updated on STN: 29 Jul 2006
Entered Medline: 28 Jul 2006

AB The existence of an immune-endocrine interaction has been reported and the modulatory effects of the natural occurring catecholamines epinephrine, norepinephrine and dopamine as well as of pharmaceutically generated catecholamines like dopexamine on a wide variety of immune functions were demonstrated. Furthermore, it was noticed that these effects are mediated by specific adrenergic and dopaminergic receptors expressed on the surface of immunological target cells. At first, the adrenergic immunomodulation was predominantly investigated in healthy volunteers and profound immunomodulatory effects were reported for endogenously released and exogenously administered catecholamines. To further elucidate the physiological significance of these interactions, investigators tried to reveal the importance of the catecholaminergic modulation of the immune system under pathological conditions like hemorrhagic shock and systemic inflammation, since catecholamines and adrenergic antagonists are frequently used drugs in the treatment of the critically ill. Furthermore, the interaction between catecholamines and the immune system is supposed to be an important factor in the development of autoimmune diseases and may influence their progress. In addition to the effects of peripheral circulating catecholamines, it was demonstrated that catecholamines that are released within the central nervous system may profoundly influence the activity of the peripheral immune system. Starting with a short historical overview over the immunomodulatory effects of blood catecholamines under good health conditions during critical illness and

during autoimmune disease will be reviewed and the immunomodulatory effects of centrally released catecholamines will be discussed.

L15 ANSWER 8 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2006341287 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16755648
TITLE: Impaired hypothalamic function, prolactinomas, and autoimmune diseases.
AUTHOR: Walker Sara E
SOURCE: The Journal of rheumatology, (2006 Jun) Vol. 33, No. 6, pp. 1036-7.
Journal code: 7501984. ISSN: 0315-162X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Commentary
Editorial
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 7 Jun 2006
Last Updated on STN: 20 Oct 2006
Entered Medline: 19 Oct 2006

L15 ANSWER 9 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2006285430 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16715039
TITLE: [Prolactin in connective tissue diseases]. Prolaktyna w ukladowych chorobach tkanki lacznej.
AUTHOR: Parada-Turska Jolanta; Targonska-Stepniak Bozena; Majdan Maria
CORPORATE SOURCE: Katedra i Klinika Reumatologii i Ukladowych Chorob Tkanki Lacznej Akademii Medycznej im. prof. Feliksa Skubiszewskiego w Lublinie.
SOURCE: Post py higieny i medycyny doswiadczalnej (Online), (2006) Vol. 60, pp. 278-85. Ref: 71
Journal code: 101206517. E-ISSN: 1732-2693.
PUB. COUNTRY: Poland
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Polish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200608
ENTRY DATE: Entered STN: 23 May 2006
Last Updated on STN: 15 Aug 2006
Entered Medline: 14 Aug 2006
AB This paper presents interactions between prolactin (PRL) and the immune system. We describe the role of PRL in the pathogenesis of rheumatic diseases, particularly connective tissue diseases, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), primary Sjogren's syndrome, systemic sclerosis, polymyalgia rheumatica, and seronegative arthritis. We present current opinion on the mechanisms responsible for hyperprolactinemia in SLE patients and the association between hyperprolactinemia and SLE activity and organ involvement. The role of dopamine receptor agonists in the treatment of connective tissue diseases is discussed.

L15 ANSWER 10 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2005628852 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16183144

TITLE: Impaired response to amphetamine and neuronal degeneration in the nucleus accumbens of autoimmune MRL-lpr mice.
AUTHOR: Anderson Kelly K; Ballok David A; Prasad Neena; Szechtman Henry; Sakic Boris
CORPORATE SOURCE: Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ont., Canada.
CONTRACT NUMBER: 1R21 AR49163-01 (NIAMS)
R21 AR049163-01 (NIAMS)
SOURCE: Behavioural brain research, (2006 Jan 6) Vol. 166, No. 1, pp. 32-8. Electronic Publication: 2005-09-23.
Journal code: 8004872. ISSN: 0166-4328.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 29 Nov 2005
Last Updated on STN: 15 Mar 2006
Entered Medline: 14 Mar 2006

AB Spontaneous development of lupus-like disease in MRL-lpr mice is accompanied by a constellation of behavioral deficits, including blunted responsiveness to sucrose. Although autoimmunity-induced damage of limbic areas is proposed to underlie this deficit, the systemic nature of the disease precludes inference of a causal relationship between CNS damage and functional loss. Based on the stimulatory effects of d-amphetamine sulfate (AMPH) on sucrose intake, the present study pharmacologically probes the functional status of central dopaminergic circuits involved in control of behavioral reward. The response rates were compared between diseased MRL-lpr mice and congenic MRL +/+ controls tested in the sucrose preference paradigm. Neuronal loss was assessed by Fluoro Jade B (FJB) staining of nucleus accumbens and the CA2/CA3 region. While control mice significantly increased intake of sucrose solutions 60 min after administration of AMPH (i.p., 0.5 mg/kg), the intake in drugged MRL-lpr mice was comparable to those given saline injection. Increased FJB staining was detected in the nucleus accumbens and hippocampus of diseased mice, and AMPH treatment neither altered this nor other measures of organ pathology. The results obtained are consistent with previously observed changes in the mesolimbic dopamine system of MRL-lpr mice and suggest that the lesion in the nucleus accumbens and deficits in dopamine release underlie impaired responsiveness to palatable stimulation during the progress of systemic autoimmune disease. As such, they point to a neurotransmitter-specific regional brain damage which may account for depressive behaviors in neuropsychiatric lupus erythematosus.

L15 ANSWER 11 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2005447513 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16114168
TITLE: A combined case of macroprolactinoma, growth hormone excess and Graves' disease.
AUTHOR: Hussein Z; Tress B; Colman P G
CORPORATE SOURCE: Department of Medicine, Hospital Putrajaya, Putrajaya, Presint 7, 62250 Malaysia.
SOURCE: The Medical journal of Malaysia, (2005 Jun) Vol. 60, No. 2, pp. 232-6.
Journal code: 0361547. ISSN: 0300-5283.
PUB. COUNTRY: Malaysia
DOCUMENT TYPE: (CASE REPORTS)

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 24 Aug 2005
Last Updated on STN: 23 Sep 2005
Entered Medline: 22 Sep 2005

AB Thyrotoxicosis due to Graves disease is a relatively common endocrine disorder. The occurrence of a prolactinoma with co-secretion of growth hormone (GH) is on the other hand, rare. We report the rare co-existence of Graves' disease in a patient with macroprolactinoma and GH hypersecretion and describe the successful response to medical therapy with dopamine agonist and antithyroid therapy. We hypothesize that hyperprolactinaemia played a role in promoting autoimmune thyroid disease in our patient and that treatment of hyperprolactinaemia may have been important in suppressing autoimmune disease activity in Graves' disease. This case also reflects on the close and complex interactions between thyroid hormones, prolactin (PRL), GH and testosterone (T).

L15 ANSWER 12 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2004338865 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15240805
TITLE: Dopamine, through the extracellular signal-regulated kinase pathway, downregulates CD4+CD25+ regulatory T-cell activity: implications for neurodegeneration.
AUTHOR: Kipnis Jonathan; Cardon Michal; Avidan Hila; Lewitus Gil M; Mordechay Sharon; Rolls Asya; Shani Yael; Schwartz Michal
CORPORATE SOURCE: Department of Neurobiology, The Weizmann Institute of Science, 76100 Rehovot, Israel.
SOURCE: The Journal of neuroscience : the official journal of the Society for Neuroscience, (2004 Jul 7) Vol. 24, No. 27, pp. 6133-43.
Journal code: 8102140. E-ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 9 Jul 2004
Last Updated on STN: 5 Feb 2005
Entered Medline: 4 Feb 2005

AB Fighting off neuronal degeneration requires a well controlled T-cell response against self-antigens residing in sites of the CNS damage. The ability to evoke this response is normally suppressed by naturally occurring CD4+CD25+ regulatory T-cells (Treg). No physiological compound that controls Treg activity has yet been identified. Here, we show that dopamine, acting via type 1 dopamine receptors (found here to be preferentially expressed by Treg), reduces the suppressive activity and the adhesive and migratory abilities of Treg. Treg activity was correlated with activation of the ERK1/2 (extracellular signal-regulated kinase 1/2) signaling pathway. Systemic injection of dopamine or an agonist of its type 1 receptors significantly enhanced, via a T-cell-dependent mechanism, protection against neuronal death after CNS mechanical and biochemical injury. These findings shed light on the physiological mechanisms controlling Treg and might open the way to novel therapeutic strategies for downregulating Treg activity (e.g., in neuronal degeneration) or for strengthening it (in autoimmune diseases).

L15 ANSWER 13 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003425695 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12965267
TITLE: Autoantibodies against four kinds of neurotransmitter receptors in psychiatric disorders.
AUTHOR: Tanaka Susumu; Matsunaga Hidenori; Kimura Masahiro; Tatsumi Ke ita; Hidaka Yoh; Takano Toru; Uema Takeshi; Takeda Masatoshi; Amino Nobuyuki
CORPORATE SOURCE: Department of Laboratory Medicine, Osaka University Graduate School of Medicine (D2), Yamada-oka 2-2, Osaka 565-0871, Suita, Japan.. tanaka@labo.med.osaka-u.ac.jp
SOURCE: Journal of neuroimmunology, (2003 Aug) Vol. 141, No. 1-2, pp. 155-64.
Journal code: 8109498. ISSN: 0165-5728.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 11 Sep 2003
Last Updated on STN: 18 Dec 2003
Entered Medline: 4 Dec 2003

AB There is a hypothesis that autoimmune abnormalities in neurotransmitter receptors might cause some psychiatric disorders. Using a sensitive radioligand assay, we detected serum autoantibodies to recombinant human muscarinic cholinergic receptor 1 (CHRM1, 34.4%), mu-opioid receptor (OPRM1, 13.1%), 5-hydroxytryptamine receptor 1A (HTR1A, 7.4%), and dopamine receptor D2 (DRD2, 4.9%) in 122 psychiatric patients. Positive antibodies to CHRM1 were found in 34.1%, 34.9%, 33.3%, and 9.1% of patients with schizophrenic disorders (n=44), mood disorders (n=63), other psychiatric disorders (n=15) and autoimmune diseases (n=33), respectively. All three patients with neuroleptic maliganant syndrome had high activities of autoantibodies to CHRM1, OPRM1, and/or HTR1A. Our data suggest that autoimmunity to neurotransmitter receptors might be associated with the induction of psychiatric symptoms and have some relation to neuroleptic malignant syndrome.

L15 ANSWER 14 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003320564 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12851722
TITLE: Autoantibodies against muscarinic cholinergic receptor in chronic fatigue syndrome.
AUTHOR: Tanaka Susumu; Kuratsune Hirohiko; Hidaka Yoh; Hakariya Yukiko; Tatsumi Ke-Ita; Takano Toru; Kanakura Yuzuru; Amino Nobuyuki
CORPORATE SOURCE: Department of Laboratory Medicine, Osaka University Graduate School of Medicine (D2), Suita-shi, Osaka 565-0871, Japan.. tanaka@labo.med.osaka-u.ac.jp
SOURCE: International journal of molecular medicine, (2003 Aug) Vol. 12, No. 2, pp. 225-30.
Journal code: 9810955. ISSN: 1107-3756.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310

ENTRY DATE: Entered STN: 10 Jul 2003
Last Updated on STN: 17 Oct 2003
Entered Medline: 16 Oct 2003

AB The disturbance of the central nervous system and immunological abnormalities have been suggested in patients with chronic fatigue syndrome (CFS). We focused on immunological abnormalities against neurotransmitter receptors in CFS. Using a sensitive radioligand assay, we examined serum autoantibodies to recombinant human muscarinic cholinergic receptor 1 (CHRM1), mu-opioid receptor (OPRM1), 5-hydroxytryptamine receptor 1A (HTR1A), and dopamine receptor D2 (DRD2) in patients with CFS (n=60) and results were compared with those in patients with autoimmune disease (n=33) and in healthy controls (n=30). The mean anti-CHRM1 antibody index was significantly higher in patients with CFS ($p<0.0001$) and autoimmune disease ($p<0.05$) than that in healthy controls, and positive reaction was found in 53.3% of patients with CFS. Anti-OPRM1 antibodies, anti-HTR1A antibodies, and anti-DRD2 antibodies were found in 15.2, 1.7, and 5.0% of patients with CFS, respectively. Anti-nuclear antibodies were found in 56.7% (34/60) of patients with CFS, but anti-nuclear antibody titers did not correlate with the activities of the above four autoantibodies. The patients with positive autoantibodies to CHRM1 had a significantly higher mean score (1.81) of 'feeling of muscle weakness' than negative patients (1.18) among CFS patients ($p<0.01$). Higher scores on 'painful node', 'forgetfulness', and 'difficulty thinking' were also found in CFS patients with anti-CHRM1 antibodies but did not reach statistical significance. In conclusion, autoantibodies to CHRM1 were detected in a large number of CFS patients and were related to CFS symptoms. Our findings suggested that subgroups of CFS are associated with autoimmune abnormalities of CHRM1.

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=> s adhesion and infiltration of leukocytes
        127046 ADHESION
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        139021 ADHESION
                  (ADHESION OR ADHESIONS)
         54393 INFILTRATION
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         56396 INFILTRATION
                  (INFILTRATION OR INFILTRATIONS)
      13734858 OF
            97 OFS
      13734858 OF
                  (OF OR OFS)
        102520 LEUKOCYTES
           311 INFILTRATION OF LEUKOCYTES
                  (INFILTRATION(W)OF(W)LEUKOCYTES)
L16          89 ADHESION AND INFILTRATION OF LEUKOCYTES

=> s l16 and autoimmune diseases
          84744 AUTOIMMUNE
             43 AUTOIMMUNES
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                  (AUTOIMMUNE OR AUTOIMMUNES)
        1748322 DISEASES
              1 DISEASESES
        1748323 DISEASES
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                (DISEASES OR DISEASESES)
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                (AUTOIMMUNE(W)DISEASES)
L17          0 L16 AND AUTOIMMUNE DISEASES

=> s l16 and autoimmune disease
         84744 AUTOIMMUNE
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       3226949 DISEASE
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         48478 AUTOIMMUNE DISEASE
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L18          1 L16 AND AUTOIMMUNE DISEASE

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L18  ANSWER 1 OF 1     MEDLINE on STN
ACCESSION NUMBER:   2003435064     MEDLINE  Full-text
DOCUMENT NUMBER:    PubMed ID: 13130482
TITLE:              Expression of myeloid-related proteins 8 and 14 in
                    systemic-onset juvenile rheumatoid arthritis.
AUTHOR:             Frosch Michael; Vogl Thomas; Seeliger Stephan; Wulffraat
                    Nico; Kuis Wietse; Viemann Dorothee; Foell Dirk; Sorg
                    Clemens; Sunderkotter Cord; Roth Johannes
CORPORATE SOURCE:   Institute of Experimental Dermatology and Department of
                    Pediatrics, University of Munster, Munster, Germany.
SOURCE:             Arthritis and rheumatism, (2003 Sep) Vol. 48, No. 9, pp.
                    2622-6.
                    Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        200310
ENTRY DATE:         Entered STN: 18 Sep 2003
                    Last Updated on STN: 18 Oct 2003
                    Entered Medline: 17 Oct 2003
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AB OBJECTIVE: To analyze which cellular compartments are involved in the initial phase of systemic-onset juvenile rheumatoid arthritis (JRA), and to investigate the role that myeloid-related protein 8 (MRP-8) and MRP-14, two S-100 proteins that are primarily expressed in phagocytes, play in the disease. METHODS: Skin biopsy samples obtained during patients' acute episodes of systemic-onset JRA were analyzed by immunohistochemistry and in situ hybridization. Concentrations of MRP-8/MRP-14 in serum were determined by enzyme-linked immunosorbent assay. RESULTS: By analyzing biopsy samples from cutaneous rashes during the initial phase of systemic-onset JRA, we discovered infiltration of leukocytes expressing MRP-8 and MRP-14. Surprisingly, keratinocytes also showed de novo synthesis of these proinflammatory proteins, indicating activation of epithelial cells during systemic-onset JRA. Serum concentrations of MRP-8/MRP-14 were 120-fold higher compared with healthy controls and approximately 12-fold higher compared with patients with other inflammatory diseases. Concentrations of MRP-8/MRP-14 in patients with systemic-onset JRA fell dramatically after remission was induced. CONCLUSION: The exceptionally high serum levels of MRP-8 and MRP-14 in active systemic-onset JRA make them prime candidates as markers for monitoring disease

activity and response to treatment. Since MRP-8/MRP-14 exhibit direct effects on leukocyte adhesion to the vascular endothelium, their extensive expression in the epidermis indicates an active role for these S-100 proteins in the initial phase of this systemic autoimmune disease.

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=> s adhesion of leukocyte
        127046 ADHESION
         17038 ADHESIONS
        139021 ADHESION
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      13734858 OF
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      13734858 OF
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        104727 LEUKOCYTE
        102520 LEUKOCYTES
        179818 LEUKOCYTE
                  (LEUKOCYTE OR LEUKOCYTES)
L19        452 ADHESION OF LEUKOCYTE
                  (ADHESION(W)OF(W)LEUKOCYTE)

=> s l19 and autoimmune disease
          84744 AUTOIMMUNE
             43 AUTOIMMUNES
          84744 AUTOIMMUNE
                  (AUTOIMMUNE OR AUTOIMMUNES)
        1952243 DISEASE
        1748322 DISEASES
        3226949 DISEASE
                  (DISEASE OR DISEASES)
          48478 AUTOIMMUNE DISEASE
                  (AUTOIMMUNE(W)DISEASE)
L20           5 L19 AND AUTOIMMUNE DISEASE

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L20  ANSWER 1 OF 5     MEDLINE on STN
ACCESSION NUMBER:   2003199508     MEDLINE  Full-text
DOCUMENT NUMBER:    PubMed ID: 12718733
TITLE:              Adhesion molecules as therapeutic targets for
                    autoimmune diseases and transplant
                    rejection.
AUTHOR:             Dedrick Russell L; Bodary Sarah; Garovoy Marvin R
CORPORATE SOURCE:   Xoma (US) LLC, 2910 Seventh Street, Berkeley, CA 94710,
                    USA.. dedrick@xoma.com
SOURCE:             Expert opinion on biological therapy, (2003 Feb) Vol. 3,
                    No. 1, pp. 85-95.  Ref: 104
                    Journal code: 101125414. ISSN: 1471-2598.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200407
ENTRY DATE:         Entered STN: 30 Apr 2003
                    Last Updated on STN: 17 Dec 2003
                    Entered Medline: 20 Jul 2004
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AB Inflammatory disorders such as autoimmune diseases and graft rejection are mediated by activated leukocytes, particularly T lymphocytes, which penetrate the inflamed tissue and perpetuate or amplify the immune reaction. In an unstimulated state, leukocytes do not readily adhere to the vascular endothelium. However, inflammatory signals induce the expression of proteins on the endothelial cell surface that promote the adhesion and extravasation of activated immune cells from the circulation into the underlying tissues. Key among these molecules are P- and E-selectin, intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) on the endothelial cells, and their respective counter receptors, P-selectin glycoprotein ligand-1 (PSGL-1), leukocyte function-associated antigen-1 (LFA-1) and very late antigen-4 (VLA-4), on the leukocytes. In vitro blockade of these molecules inhibits the adhesion of leukocytes. In many cases there is attenuation of leukocyte activation as well. Adhesion blockade in animal models prevents or ameliorates graft rejection and disease severity in autoimmune models. Clinical studies with humanised monoclonal antibodies which interfere with LFA-1/ICAM-1 or VLA-4/VCAM-1 interactions have shown significant efficacy and good safety profiles in autoimmune disease, including psoriasis, multiple sclerosis and inflammatory bowel disease. Thus, adhesion blockade is emerging as a useful therapeutic strategy in several inflammatory settings.

L20 ANSWER 2 OF 5 MEDLINE on STN
ACCESSION NUMBER: 2002741738 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12506079
TITLE: Leukocyte trafficking in experimental autoimmune uveitis: breakdown of blood-retinal barrier and upregulation of cellular adhesion molecules.
AUTHOR: Xu Heping; Forrester John V; Liversidge Janet; Crane Isabel J
CORPORATE SOURCE: Department of Ophthalmology, Aberdeen University Medical School, Foresterhill, Aberdeen AB25 2ZD, Scotland, United Kingdom.. h.xu@abdn.ac.uk
SOURCE: Investigative ophthalmology & visual science, (2003 Jan) Vol. 44, No. 1, pp. 226-34.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 31 Dec 2002
Last Updated on STN: 14 Jan 2003
Entered Medline: 13 Jan 2003

AB PURPOSE: To clarify the order of events occurring in the breakdown of the blood-retinal barrier (BRB) in experimental autoimmune uveoretinitis (EAU) and in particular to study the relationships between increased vascular permeability, upregulation of endothelial cell adhesion molecules, and leukocyte adhesion and infiltration during EAU. METHODS: B10.RIII mice were immunized with human interphotoreceptor retinoid binding protein (IRBP) peptide 161-180. Changes in the retinal microvasculature were examined on days 3, 6, 7, 8, 9, 10, 16, and 21 postimmunization (pi). Evans blue dye was administered intravenously to assess vascular permeability. Expression of intercellular adhesion molecule (ICAM)-1, vascular cell adhesion molecule (VCAM)-1, P-selectin, E-selectin, and platelet endothelial cell adhesion molecule (PECAM)-1 was evaluated by in vivo administration of antibody and subsequent immunostaining of retinal wholemounts. Lymphocytes from inguinal lymph nodes of normal and chicken ovalbumin (OVA)- or IRBP peptide-immunized mice at day 5, 6, 7, 8, and 15 pi were labeled in vitro with calcein-AM (C-AM)

and infused intravenously into syngeneic recipient mice, which had been immunized with peptide at the same corresponding time point. Wholemount preparations of retinas were observed 24 hours later by confocal microscopy to determine the adhesion and infiltration of lymphocytes. RESULTS: The first observation of an increase in vascular permeability occurred at day 7 pi and was restricted to focal areas of the retinal postcapillary venules of the inner vascular plexus. This progressively extended to the outer vascular plexus at day 9 pi. Specific adhesion of leukocytes to the endothelium of retinal venules of the inner vascular plexus was first observed at day 6 pi. Leukocyte extravasation into the retinal parenchyma from these vessels began at day 8 pi and extended to the outer vascular plexus at day 9 pi. The expression of adhesion molecules increased progressively during the development of EAU. In particular, the adhesion molecules ICAM-1, P-selectin, and E-selectin were expressed predominately in retinal venules, the sites of BRB breakdown, cell adhesion, and extravasation, from day 7 pi. The increases in expression of ICAM-1 and P-selectin were associated both spatially and temporally with breakdown of the BRB, cell adhesion, and extravasation. No increase in expression of P-selectin and ICAM-1 was observed in either the mesenteric vessels of EAU mice or the retinal vessels of OVA-immunized mice. CONCLUSIONS: The sequence of events in EAU appears to be focal adhesion of leukocytes to discrete sites on postcapillary venules, followed by upregulation of adhesion molecules, especially ICAM-1 and P-selectin, and breakdown of the BRB, leading to transendothelial migration of leukocytes and recruitment of large numbers of cells to the retinal parenchyma. These changes occur over a short period of 6 to 9 days pi and initiate the process of tissue damage during the following 2 to 3 weeks.

L20 ANSWER 3 OF 5 MEDLINE on STN
ACCESSION NUMBER: 2000115223 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10648114
TITLE: The inhibitory effects of transforming growth factor-beta-1 (TGF-beta1) in autoimmune diseases.
AUTHOR: Prud'homme G J; Piccirillo C A
CORPORATE SOURCE: Department of Pathology, McGill University, 3775 University St., Room B13, Montreal, Quebec, H3A 2B4, Canada..
Prudhomm@pathology.lanmcgill.ca
SOURCE: Journal of autoimmunity, (2000 Feb) Vol. 14, No. 1, pp. 23-42. Ref: 235
Journal code: 8812164. ISSN: 0896-8411.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 30 Mar 2000
Last Updated on STN: 30 Mar 2000
Entered Medline: 20 Mar 2000

AB The importance of transforming growth factor-beta-1 (TGF-beta1) in immunoregulation and tolerance has been increasingly recognized. It is now proposed that there are populations of regulatory T cells (T-reg), some designated T-helper type 3 (Th3), that exert their action primarily by secreting this cytokine. Here, we emphasize the following concepts: (1) TGF-beta1 has multiple suppressive actions on T cells, B cells, macrophages, and other cells, and increased TGF-beta1 production correlates with protection and/or recovery from autoimmune diseases; (2) TGF-beta1 and CTLA-4 are molecules that work together to terminate immune responses; (3) Th0, Th1 and Th2 clones can all secrete TGF-beta1 upon cross-linking of CTLA-4 (the

functional significance of this in autoimmune diseases has not been reported, but TGF-beta1-producing regulatory T-cell clones can produce type 1 inflammatory cytokines); (4) TGF-beta1 may play a role in the passage from effector to memory T cells; (5) TGF-beta1 acts with some other inhibitory molecules to maintain a state of tolerance, which is most evident in immunologically privileged sites, but may also be important in other organs; (6) TGF-beta1 is produced by many cell types, is always present in the plasma (in its latent form) and permeates all organs, binding to matrix components and creating a reservoir of this immunosuppressive molecule; and (7) TGF-beta1 downregulates adhesion molecules and inhibits adhesion of leukocytes to endothelial cells. We propose that rather than being passive targets of autoimmunity, tissues and organs actively suppress autoreactive lymphocytes. We review the beneficial effects of administering TGF-beta1 in several autoimmune diseases, and show that it can be effectively administered by a somatic gene therapy approach, which results in depressed inflammatory cytokine production and increased endogenous regulatory cytokine production.

L20 ANSWER 4 OF 5 MEDLINE on STN
ACCESSION NUMBER: 97389373 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9265500
TITLE: Humanization of a mouse antibody against human alpha-4 integrin: a potential therapeutic for the treatment of multiple sclerosis.
AUTHOR: Leger O J; Yednock T A; Tanner L; Horner H C; Hines D K; Keen S; Saldanha J; Jones S T; Fritz L C; Bendig M M
CORPORATE SOURCE: MRC Collaborative Centre, London, UK.
SOURCE: Human antibodies, (1997) Vol. 8, No. 1, pp. 3-16. Journal code: 9711270. ISSN: 1093-2607.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X93023; GENBANK-X93024
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 8 Oct 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 22 Sep 1997

AB alpha 4 beta 1 integrin (VLA-4) is crucial for the adhesion of leukocytes to human vascular cell adhesion molecule-1 (VCAM-1) on inflamed endothelium. This cell adhesion event is the first step in leukocyte extravasation across the blood-brain barrier in inflammatory diseases of the central nervous system (CNS) such as experimental autoimmune encephalomyelitis (EAE). Prevention of leukocyte infiltration by antibodies against the alpha 4 integrin, which block the alpha 4 beta 1 integrin/VCAM-1 interaction, have been shown to suppress clinical and pathological features of EAE. In this study, two mouse monoclonal antibodies (MAb) directed against human alpha 4 integrin were analyzed in vitro for their ability to block the interaction of leukocytes with VCAM-1 under different assay conditions. The best blocking MAb, AN100226m, was humanized by complementarily-determining region grafting, associated with human C regions and expressed. We found that modification of two structural determinants (H27 and H29) for the heavy chain CDR1 loop in one hand, and modification of framework amino acid H38, H40 and H44 in the other hand, had no effect on antigen binding. In contrast, modification of a structural determinant (H71) for the heavy chain CDR2 loop resulted in loss of binding. The humanized antibody. AN100226, was equivalent to the murine antibody. AN100226m, in binding to alpha 4 beta 1 integrin and in blocking cell adhesion. More importantly, AN100226 was as effective as AN100226m in the reversal of active EAE in guinea pigs and thus may be useful in the

treatment of autoimmune diseases such as multiple sclerosis. AN100226 is currently in phase II clinical trials in the UK for the treatment of multiple sclerosis exacerbations.

L20 ANSWER 5 OF 5 MEDLINE on STN
ACCESSION NUMBER: 97294803 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9150476
TITLE: Mycophenolate mofetil limits renal damage and prolongs life in murine lupus autoimmune disease.
AUTHOR: Corna D; Morigi M; Facchinetti D; Bertani T; Zoja C; Remuzzi G
CORPORATE SOURCE: Mario Negri Institute for Pharmacological Research, Bergamo, Italy.
SOURCE: Kidney international, (1997 May) Vol. 51, No. 5, pp. 1583-9.
Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 21 Jul 1997
Last Updated on STN: 21 Jul 1997
Entered Medline: 3 Jul 1997

AB Classical immunosuppressants like cyclophosphamide give excellent results in human lupus nephritis. However, they augment malignancies and viral infections. Here we investigated the effect of the new immunosuppressant agent, mycophenolate mofetil (MMF), in New Zealand Black x New Zealand White (NZBxW) F1 hybrid mice, a model of genetically determined immune complex disease that mimics systemic lupus in humans. MMF has a selective antiproliferative effect on T- and B-lymphocytes, inhibits antibody formation and blocks the glycosylation of lymphocyte glycoproteins involved in the adhesion of leukocytes to endothelial cells. Two groups of NZBxW mice were used: group 1 (N = 20) given daily MMF (60 mg/kg p.o.) and group 2 (N = 15) given daily vehicle alone. Treatment started at three months of age and lasted until the death of the animals. Results showed that percentage of proteinuric mice was significantly reduced by MMF treatment and serum BUN levels were also lower than vehicle. MMF had a suppressive effect on autoantibody production and protected animals from leukopenia and anemia. Life survival of MMF treated lupus mice was significantly improved in respect to untreated animals. Thus, MMF delayed renal function deterioration and prolonged life survival in murine lupus nephritis. MMF has been already recognized as reasonably well tolerated in renal transplant patients and despite its gastrointestinal toxicity its overall safety profile appears superior to azathioprine. Human studies are needed to establish whether MMF may function as a steroid-sparing drug in lupus nephritis.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	45.30	122.24

FILE 'STNGUIDE' ENTERED AT 15:10:10 ON 13 NOV 2007

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Nov  9, 2007 (20071109/UP).

=> s cell adhesion inhibitory
            15 CELL
             0 ADHESION
             0 INHIBITORY
L21          0 CELL ADHESION INHIBITORY
                 (CELL(W)ADHESION(W)INHIBITORY)

=> s cell infiltration inhibitory
            15 CELL
             0 INFILTRATION
             0 INHIBITORY
L22          0 CELL INFILTRATION INHIBITORY
                 (CELL(W)INFILTRATION(W)INHIBITORY)

=> s cell infiltration inhibit!@
            15 CELL
             0 INFILTRATION
             0 INHIBIT!
L23          0 CELL INFILTRATION INHIBIT!@
                 (CELL(W)INFILTRATION(W)INHIBIT!)

=> s cell infiltration inhibit!
            15 CELL
             0 INFILTRATION
             0 INHIBIT!
L24          0 CELL INFILTRATION INHIBIT!
                 (CELL(W)INFILTRATION(W)INHIBIT!)

=> file medline
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.90     123.14

FILE 'MEDLINE' ENTERED AT 15:19:19 ON 13 NOV 2007

 FILE LAST UPDATED: 10 Nov 2007 (20071110/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s cell infiltration inhibit!
       2190278 CELL
       1978654 CELLS
       2907941 CELL
                 (CELL OR CELLS)
         54393 INFILTRATION
          2527 INFILTRATIONS
         56396 INFILTRATION
                 (INFILTRATION OR INFILTRATIONS)
        110079 INHIBIT!
L25          0 CELL INFILTRATION INHIBIT!
                 (CELL(W)INFILTRATION(W)INHIBIT!)

=> s cell adhesion inhibit!
       2190278 CELL
       1978654 CELLS
       2907941 CELL
```

```
                (CELL OR CELLS)
        127046 ADHESION
         17038 ADHESIONS
        139021 ADHESION
                (ADHESION OR ADHESIONS)
        110079 INHIBIT!
L26          4 CELL ADHESION INHIBIT!
                (CELL(W)ADHESION(W)INHIBIT!)

=> s l26 and autoimmune disease
         84744 AUTOIMMUNE
            43 AUTOIMMUNES
         84744 AUTOIMMUNE
                (AUTOIMMUNE OR AUTOIMMUNES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                (DISEASE OR DISEASES)
         48478 AUTOIMMUNE DISEASE
                (AUTOIMMUNE(W)DISEASE)
L27          0 L26 AND AUTOIMMUNE DISEASE

=> s l26 and inflammatory disease
        284191 INFLAMMATORY
           329 INFLAMMATORIES
        284330 INFLAMMATORY
                (INFLAMMATORY OR INFLAMMATORIES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                (DISEASE OR DISEASES)
         21094 INFLAMMATORY DISEASE
                (INFLAMMATORY(W)DISEASE)
L28          0 L26 AND INFLAMMATORY DISEASE

=> s l1 and inflammatory disease
             0 L1
        284191 INFLAMMATORY
           329 INFLAMMATORIES
        284330 INFLAMMATORY
                (INFLAMMATORY OR INFLAMMATORIES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                (DISEASE OR DISEASES)
         21094 INFLAMMATORY DISEASE
                (INFLAMMATORY(W)DISEASE)
L29          0 L1 AND INFLAMMATORY DISEASE

=> s l5 and inflammatory disease
        284191 INFLAMMATORY
           329 INFLAMMATORIES
        284330 INFLAMMATORY
                (INFLAMMATORY OR INFLAMMATORIES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                (DISEASE OR DISEASES)
         21094 INFLAMMATORY DISEASE
                (INFLAMMATORY(W)DISEASE)
```

```
L30          0 L5 AND INFLAMMATORY DISEASE

=> file medlinme
'MEDLINME' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'MEDLINE'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.44     125.58

FILE 'MEDLINE' ENTERED AT 15:22:45 ON 13 NOV 2007

 FILE LAST UPDATED: 10 Nov 2007 (20071110/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l7 and inflammatory disease
        284191 INFLAMMATORY
           329 INFLAMMATORIES
        284330 INFLAMMATORY
                  (INFLAMMATORY OR INFLAMMATORIES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                  (DISEASE OR DISEASES)
         21094 INFLAMMATORY DISEASE
                  (INFLAMMATORY(W)DISEASE)
L31          0 L7 AND INFLAMMATORY DISEASE

=> s l13 and inflammatory disease
        284191 INFLAMMATORY
           329 INFLAMMATORIES
        284330 INFLAMMATORY
                  (INFLAMMATORY OR INFLAMMATORIES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                  (DISEASE OR DISEASES)
         21094 INFLAMMATORY DISEASE
                  (INFLAMMATORY(W)DISEASE)
L32          9 L13 AND INFLAMMATORY DISEASE

=> d ibib abs tot

L32  ANSWER 1 OF 9     MEDLINE on STN
ACCESSION NUMBER:   2007195384     MEDLINE  Full-text
DOCUMENT NUMBER:    PubMed ID: 17320857
TITLE:              Anti-inflammatory and analgesic effects of the
                    sesquiterpene lactone budlein A in mice: inhibition of
                    cytokine production-dependent mechanism.
AUTHOR:             Valerio Daniel A R; Cunha Thiago M; Arakawa Nilton S; Lemos
                    Henrique P; Da Costa Fernando B; Parada Carlos A; Ferreira
                    Sergio H; Cunha Fernando Q; Verri Waldiceu A Jr
CORPORATE SOURCE:   Department of Pharmacology, School of Medicine of Ribeirao
```

Preto, University of Sao Paulo, Sao Paulo, Avenida Bandeirantes, 3900, 14049-900-Ribeirao Preto, Sao Paulo, Brazil.

SOURCE: European journal of pharmacology, (2007 May 7) Vol. 562, No. 1-2, pp. 155-63. Electronic Publication: 2007-02-01. Journal code: 1254354. ISSN: 0014-2999.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200706

ENTRY DATE: Entered STN: 3 Apr 2007
Last Updated on STN: 14 Jun 2007
Entered Medline: 13 Jun 2007

AB The anti-inflammatory activities of some medicinal plants are attributed to their contents of sesquiterpene lactones. In the present study, the anti-inflammatory and anti-nociceptive activity of a sesquiterpene lactone isolated from Viguiera robusta, budlein A in mice was investigated. The treatment with budlein A dose--(1.0-10.0 mg/kg, p.o., respectively) dependently inhibited the carrageenan-induced: i. neutrophil migration to the peritoneal cavity (2-52%), ii. neutrophil migration to the paw skin tissue (32-74%), iii. paw oedema (13-74%) and iv. mechanical hypernociception (2-58%) as well as the acetic acid-induced writhings (0-66%). Additionally, budlein A (10.0 mg/kg) treatment inhibited the mechanical hypernociception-induced by tumour necrosis factor (TNF-alpha, 36%), Keratinocyte-derived chemokine (KC, 37%) and Interleukin-1beta (IL-1beta, 28%), but not of prostaglandin E(2) or dopamine. Budlein A also inhibited the carrageenan-induced release of TNF-alpha (52%), KC (70%) and IL-1beta (59%). Furthermore, an 8 days treatment with budlein A inhibited Complete Freund's adjuvant (10 microl/paw)-induced hypernociception, paw oedema and paw skin myeloperoxidase activity increase while not affecting the motor performance or myeloperoxidase activity in the stomach. Concluding, the present data suggest that budlein A presents anti-inflammatory and antinociceptive property in mice by a mechanism dependent on inhibition of cytokines production. It supports the potential beneficial effect of orally administered budlein A in inflammatory diseases involving cytokine-mediated nociception, oedema and neutrophil migration.

L32 ANSWER 2 OF 9 MEDLINE on STN

ACCESSION NUMBER: 2006697293 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 17136226

TITLE: Bupropion.

AUTHOR: Wilkes Scott

CORPORATE SOURCE: Centre for Primary and Community Care, School of Health, Natural & Social Sciences, University of Sunderland, Sunderland, UK.. scott.wilkes@sunderland.ac.uk

SOURCE: Drugs of today (Barcelona, Spain : 1998), (2006 Oct) Vol. 42, No. 10, pp. 671-81. Ref: 83
Journal code: 101160518. ISSN: 1699-3993.

PUB. COUNTRY: Spain

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200705

ENTRY DATE: Entered STN: 1 Dec 2006
Last Updated on STN: 4 May 2007
Entered Medline: 3 May 2007

AB Bupropion was initially developed and licensed for the treatment of major depressive disorder in the United States in 1989. It was licensed as a pharmacotherapy for smoking cessation in the United States in 1997 and in the United Kingdom in 2000, and for the prevention of seasonal major depressive episodes in patients with seasonal affective disorder in the United States in 2006. Its main mechanism of action is believed to be via dopamine and noradrenalin reuptake inhibition. In addition to proven clinical efficacy for the treatment of major depression, the prevention of depressive episodes in patients with seasonal affective disorder, and as an aid to smoking cessation treatment, bupropion has demonstrated efficacy for attenuation of symptoms of attention deficit hyperactivity disorder, and more recently it has shown anti-inflammatory action against proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha), which may be implicated in a number of inflammatory diseases such as Crohn's disease. The twice-daily sustained-release formulation has been extensively evaluated for smoking cessation and has shown continuous smoking abstinence rates at one year of the order of 20% across many clinical groups including healthy smokers, and smokers with cardiovascular disease, chronic obstructive airways disease, depression and schizophrenia. Bupropion is well tolerated with side effects including insomnia, headache, dry mouth, dizziness and nausea. Bupropion is a cytochrome p450 2D6 inhibitor and care must be taken when coprescribing with drugs cleared by this enzyme and when coprescribing with drugs that lower seizure threshold. Despite the clinical effectiveness and cost-effectiveness of bupropion as an aid to smoking cessation, its uptake for this indication remains low when compared with nicotine replacement therapy.

L32 ANSWER 3 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2006654968 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16912126
TITLE: Effects of chronic osteoarthritis pain on neuroendocrine function in men.
AUTHOR: Khoromi Suzan; Muniyappa Ranganath; Nackers Lisa; Gray Nora; Baldwin Howard; Wong Kelli Anne; Matheny Leigh Ann; Moquin Barbara; Rainer Aliya; Hill Suvimol; Remaley Alan; Johnson Laura Lee; Max Mitchell B; Blackman Marc R
CORPORATE SOURCE: Laboratory of Clinical Investigation, Division of Intramural Research, National Center for Complementary and Alternative Medicine, National Institutes of Health, Bethesda, Maryland 20892-1302, USA.. khoromisu@mail.nih.gov
SOURCE: The Journal of clinical endocrinology and metabolism, (2006 Nov) Vol. 91, No. 11, pp. 4313-8. Electronic Publication: 2006-08-15.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., INTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 8 Nov 2006
Last Updated on STN: 13 Jan 2007
Entered Medline: 12 Jan 2007

AB CONTEXT: Chronic pain has been associated with elevated cortisol, reduced LH and testosterone (T), and/or augmented circulating or excreted catecholamines. Most endocrine studies have been conducted in patients in whom the potentially confounding effects of depression, inflammatory disease, or coexistent medication use have not been controlled. OBJECTIVE: The objective of the study was to test the hypothesis that chronic pain activates ACTH-cortisol and

suppresses LH-T. DESIGN AND SETTING: This was a case control study conducted at a clinical research center. PARTICIPANTS: Participants included 16 opioid-naive men with chronic osteoarthritis pain, aged 35-65 yr with body mass index 20-30 kg/m2, and 12 healthy, opioid- and pain-free men of similar ages and body mass indexes. METHODS: We compared circulating concentrations of ACTH, cortisol, LH, and T derived from every 20-min blood sampling (2000-0800 h), and 24-h urinary excretion of cortisol, epinephrine, norepinephrine, and dopamine. RESULTS: There were no significant differences in mean or integrated concentrations of ACTH, cortisol, LH, or T, or in the corresponding approximate entropy scores in osteoarthritis patients, compared with control subjects. The 0800-h serum LH concentrations were elevated in patients vs. controls (6.42 +/- 1.65 vs. 3.99 +/- 1.54 IU/liter, mean +/- sd, P = 0.02), whereas there were no significant group differences in total or free T, SHBG, cortisol binding globulin, dehydroepiandrosterone sulfate, or urinary cortisol and catecholamines. CONCLUSIONS: These data suggest that neuroendocrine function is not significantly altered in otherwise healthy men with chronic musculoskeletal pain and that prior reports of such hormonal abnormalities may have resulted from the confounding effects of coexistent illness or medication use.

L32 ANSWER 4 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2005177133 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15751003
TITLE: Proteomic changes in rat serum, polymorphonuclear and mononuclear leukocytes after chronic nicotine administration.
AUTHOR: Piubelli Chiara; Cecconi Daniela; Astner Hubert; Caldara Fabrizio; Tessari Michela; Carboni Lucia; Hamdan Mahmoud; Righetti Pier Giorgio; Domenici Enrico
CORPORATE SOURCE: Department of Agricultural and Industrial Biotechnologies, University of Verona, Verona, Italy.
SOURCE: Proteomics, (2005 Apr) Vol. 5, No. 5, pp. 1382-94. Journal code: 101092707. ISSN: 1615-9853.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 6 Apr 2005
Last Updated on STN: 1 Oct 2005
Entered Medline: 30 Sep 2005

AB In order to gain information about the effect triggered at the molecular level by nicotine, its neuroimmunomodulatory properties and its impact on the pathogenesis of inflammatory diseases, peripheral blood serum and leukocytes of rat submitted to passive nicotine administration were subjected to proteomic investigation. Serum, polymorphonuclear (PMN) and mononuclear (MN) leukocytes from chronically treated animals and from control animals were analysed by a two-dimensional (2-D) gel electrophoresis/mass spectrometry approach to detect differentially expressed proteins. The nicotine regimen selected is known to have a stimulatory effect on locomotor activity and to produce a sensitisation of the mesolimbic dopamine system mechanism involved in addiction development. After 2-D gel analysis and matching, 36 spots in serum, seven in PMN and five in MN were found to display a statistical difference in their expression and were subjected to matrix-assisted laser desorption/ionization-time of flight-mass spectrometry peptide fingerprinting for protein identification. Fifteen different proteins were identified. The results indicate an overall impact of nicotine on proteins involved in a variety of cellular and metabolic pathways, including acute phase response

(suggesting the effect on inflammatory cascades and more in general on the immune system), oxidative stress metabolism and assembly and regulation of cytoskeleton. In particular, the observed changes imply a general reduction in the inflammatory response with a concomitant increased unbalance of the oxidative stress metabolism in the periphery and point to a number of potential noninvasive markers for the central nervous system (CNS) and non-CNS mediated activities of nicotine.

L32 ANSWER 5 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2004081761 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14764703
TITLE: Immunosuppressive activity of endovanilloids: N-arachidonoyl-dopamine inhibits activation of the NF-kappa B, NFAT, and activator protein 1 signaling pathways.
AUTHOR: Sancho Rocio; Macho Antonio; de La Vega Laureano; Calzado Marco A; Fiebich Bernd L; Appendino Giovanni; Munoz Eduardo
CORPORATE SOURCE: Departamento de Biologia Celular, Fisiologia e Inmunologia, Universidad de Cordoba, Facultad de Medicina, Cordoba, Spain.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Feb 15) Vol. 172, No. 4, pp. 2341-51.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 16 Jun 2004
Entered Medline: 15 Jun 2004

AB Endogenous N-acyl dopamines such as N-arachidonoyldopamine (NADA) and N-oleoyldopamine have been recently identified as a new class of brain neurotransmitters sharing endocannabinoid and endovanilloid biological activities. As endocannabinoids show immunomodulatory activity, and T cells play a key role in the onset of several diseases that affect the CNS, we have evaluated the immunosuppressive activity of NADA and N-oleoyldopamine in human T cells, discovering that both compounds are potent inhibitors of early and late events in TCR-mediated T cell activation. Moreover, we found that NADA specifically inhibited both IL-2 and TNF-alpha gene transcription in stimulated Jurkat T cells. To further characterize the inhibitory mechanisms of NADA at the transcriptional level, we examined the DNA binding and transcriptional activities of NF-kappaB, NF-AT, and AP-1 transcription factors in Jurkat cells. We found that NADA inhibited NF-kappaB-dependent transcriptional activity without affecting either degradation of the cytoplasmic NF-kappaB inhibitory protein, IkappaBalpha, or DNA binding activity. However, phosphorylation of the p65/RelA subunit was clearly inhibited by NADA in stimulated cells. In addition, NADA inhibited both binding to DNA and the transcriptional activity of NF-AT and AP-1, as expected from the inhibition of NF-AT1 dephosphorylation and c-Jun N-terminal kinase activation in stimulated T cells. Finally, overexpression of a constitutively active form of calcineurin demonstrated that this phosphatase may represent one of the main targets of NADA. These findings provide new mechanistic insights into the anti-inflammatory activities of NADA and highlight their potential to design novel therapeutic strategies to manage inflammatory diseases.

L32 ANSWER 6 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2001698660 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11744348
TITLE: Is obesity an inflammatory condition?.
AUTHOR: Das U N
CORPORATE SOURCE: EFA Sciences LLC, Norwood, Massachusets 02062, USA.. undurti@hotmail.com
SOURCE: Nutrition (Burbank, Los Angeles County, Calif.), (2001 Nov-Dec) Vol. 17, No. 11-12, pp. 953-66. Ref: 230 Journal code: 8802712. ISSN: 0899-9007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 18 Dec 2001 Last Updated on STN: 29 Apr 2002 Entered Medline: 26 Apr 2002

AB Obesity may be a low-grade systemic inflammatory disease . Overweight and obese children and adults have elevated serum levels of C-reactive protein, interleukin-6, tumor necrosis factor-alpha, and leptin, which are known markers of inflammation and closely associated with cardiovascular risk factors and cardiovascular and non-cardiovascular causes of death. This may explain the increased risk of diabetes, heart disease, and many other chronic diseases in the obese. The complex interaction between several neurotransmitters such as dopamine, serotonin, neuropeptide Y, leptin, acetylcholine, melanin-concentrating hormone, ghrelin, nitric oxide, and cytokines and insulin and insulin receptors in the brain ultimately determines and regulates food intake. Breast-feeding of more than 12 mo is associated with decreased incidence of obesity. Breast milk is a rich source of long-chain polyunsaturated fatty acids (LCPUFAs) and brain is especially rich in these fatty acids. LCPUFAs inhibit the production of proinflammatory cytokines and enhance the number of insulin receptors in various tissues and the actions of insulin and several neurotransmitters. LCPUFAs may enhance the production of bone morphogenetic proteins, which participate in neurogenesis, so these fatty acids might play an important role in brain development and function. It is proposed that obesity is a result of inadequate breast feeding, which results in marginal deficiency of LCPUFAs during the critical stages of brain development. This results in an imbalance in the structure, function, and feedback loops among various neurotransmitters and their receptors, which ultimately leads to a decrease in the number of dopamine and insulin receptors in the brain. Hence, promoting prolonged breast feeding may decrease the prevalence of obesity. Exercise enhances parasympathetic tone, promotes antiinflammation, and augments brain acetylcholine and dopamine levels, events that suppress appetite. Acetylcholine and insulin inhibit the production of proinflammatory cytokines and provide a negative feedback loop for postprandial inhibition of food intake, in part, by regulating leptin action. Statins, peroxisome proliferator-activated receptor-gamma binding agents, non-steroidal antiinflammatory drugs, and infant formulas supplemented with LCPUFAs, and LCPUFAs themselves, which suppress inflammation, may be beneficial in obesity.

L32 ANSWER 7 OF 9 MEDLINE on STN
ACCESSION NUMBER: 94006618 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1339601
TITLE: [Present possibilities of therapy of septic shock in surgical patients].
Soucasne moznosti v terapii septickeho soku u chirurgickych

nemocnych.
AUTHOR: Vyhnanek F; Lochmann O
CORPORATE SOURCE: Chirurgicka klinika 3. lekarske fakulty Univerzity Karlovy, Praha.
SOURCE: Ceskoslovenska epidemiologie, mikrobiologie, imunologie, (1992 Sep) Vol. 42, No. 3, pp. 105-15.
Journal code: 2984708R. ISSN: 0009-0522.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Czech
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 17 Jan 1994
Last Updated on STN: 6 Feb 1998
Entered Medline: 23 Nov 1993

AB The authors present a review of contemporary possibilities of septic shock in surgical patients. As mentioned by the authors, the most frequent cause of Gram-negative sepsis in surgery are intraabdominal inflammatory diseases or septic complications after planned surgery. Based on an experimental study on acute endotoxin shock in dogs and treatment with hydrocortisone, dopamine and antihypertensive drugs (mepamil and metazosine), the authors present some principles of the therapeutic procedure in endotoxin shock under clinical conditions. They emphasize in particular administration of antibodies against endotoxin and cytokines. In the clinical part they submit results of comprehensive therapy of intraabdominal sepsis in patients hospitalized at the intensive care unit of the Surgical Clinic at the Third Medical Faculty in Prague. They give an account of the principles of peroperative and postoperative treatment within the framework of differentiated care. During the postoperative period it is important to ensure prevention and treatment of septic complications such as septic shock and the syndrome of multiorgan systemic failure as well as rational antimicrobial therapy, immunotherapy and adequate nutrition. The authors emphasize that it is essential that specific antibodies are available and indications of their administration must be defined. The expected effect of immunotherapy is limited by the period of administration in relation to early stages of sepsis.

L32 ANSWER 8 OF 9 MEDLINE on STN
ACCESSION NUMBER: 93392087 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8378882
TITLE: [Breast feeding, lactation disorders and inflammatory diseases of the female breast].
Stillen, Stillschwierigkeiten und entzundliche Erkrankungen der weiblichen Brust.
AUTHOR: Schneider H P; Raber G
CORPORATE SOURCE: Zentrum fur Frauenheilkunde, Westfalische Wilhelms-Universitat Munster.
SOURCE: Therapeutische Umschau. Revue therapeutique, (1993 May) Vol. 50, No. 5, pp. 280-5. Ref: 11
Journal code: 0407224. ISSN: 0040-5930.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 5 Nov 1993

Last Updated on STN: 5 Nov 1993
Entered Medline: 21 Oct 1993

AB Approximately 98% of our female population are capable of breast-feeding. Optimal success in breast-feeding is achieved when the first suckling stimulus occurs no later than 2 h following delivery. Obstetrical surgery impairs breast-feeding. Lactation is considered to be optimal with 7 to 10 min of milk uptake and 7 to 10 min of suckling for galactopoesis and discontinuation. The individual pattern of suckling is critical for initiation and duration of lactation. Due to environmental contamination of the milk, a critical assessment of advantages and disadvantages of breast-feeding needs to be performed if it is considered for more than four months. Early diagnosis and immediate initiation of treatment of mastitis helps avoiding abscess formation with potential surgical sequelae. Medical--dopamine agonists--and physical therapy permit continuation of breast-feeding.

L32 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 92171298 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1539899
TITLE: Ruptured ectopic pregnancy in a patient with a recent intrauterine abortion.
AUTHOR: Nugent P J
CORPORATE SOURCE: Bethesda Hospitals, Cincinnati, Ohio.
SOURCE: Annals of emergency medicine, (1992 Jan) Vol. 21, No. 1, pp. 97-9.
Journal code: 8002646. ISSN: 0196-0644.
Report No.: PIP-075557; POP-00214978.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Population
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 17 Apr 1992
Last Updated on STN: 1 Nov 2002
Entered Medline: 31 Mar 1992

AB The case of a 33-year-old woman who presented with abdominal pain referable to the lower abdomen is discussed. She had had an uncomplicated intrauterine abortive procedure two weeks earlier. It was determined that a ruptured ectopic pregnancy was the etiology of her abdominal pain. The rare phenomenon of combined intrauterine and extrauterine pregnancy is discussed. In Ohio, a 33-year old woman who had never had an ectopic pregnancy presented at an emergency facility not physically attached to a hospital with abdominal pain over 24 hours which had become more intense during the preceding 4 hours. She did not have vaginal bleeding, diarrhea, vomiting, or pain while urinating. 2 weeks earlier she had a voluntary intrauterine abortion at 8 weeks' gestation. She had intercourse 1 week before coming to the emergency facility. She had widespread tenderness in her abdomen, especially in the lower areas. Blood cell studies suggested an infection. The attending physician presumed her to have pelvic inflammatory disease (PID) as a result of either sexual intercourse or the elective abortion. The physician called for a urinary beta human chorionic gonadotropin test to determine whether placental tissue remained in the uterus. It was positive. 60 minutes after admission, the supine patient's pain increased and her blood pressure dropped to 80/50 mm Hg from 100/60 mm Hg at admission. After administering Ringer's solution, the health team sat her up and she fainted. A repeat cell count indicated sepsis. Her blood pressure decreased to 60 by Doppler and the physician continued to give her fluids and began dopamine. After the team stabilized her, they transferred her to a hospital. Her private physician examined her and then

began surgery. The physician found a tubal pregnancy and removed the affected tube and ovary. She recuperated completely. Combined intrauterine and extrauterine pregnancy occurs once in every 30,000 cases. Previous PID, use of ovulation inducing medication, and in vitro fertilization with embryo transfer increases the likelihood of this type of pregnancy occurring. Physicians should consider this possibility if a woman has any of these histories and a combination of abdominal pain, adnexal mass with pain and tenderness, peritoneal irritation, and an enlarged uterus.

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=> s l19 and inflammatory disease
        284191 INFLAMMATORY
           329 INFLAMMATORIES
        284330 INFLAMMATORY
                  (INFLAMMATORY OR INFLAMMATORIES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                  (DISEASE OR DISEASES)
         21094 INFLAMMATORY DISEASE
                  (INFLAMMATORY(W)DISEASE)
L33         17 L19 AND INFLAMMATORY DISEASE

=> d ibib abs tot

L33  ANSWER 1 OF 17     MEDLINE on STN
ACCESSION NUMBER:   2007443027     IN-PROCESS  Full-text
DOCUMENT NUMBER:    PubMed ID: 17659431
TITLE:              Modulation of the inflammatory response by estrogens with
                    focus on the endothelium and its interactions with
                    leukocytes.
AUTHOR:             Nilsson B-O
CORPORATE SOURCE:   Department of Experimental Medical Science, Division of
                    Vascular and Airway Research, Unit of Vascular Physiology,
                    Lund University, BMC D12, 221 84 Lund, Sweden.
SOURCE:             Inflammation research : official journal of the European
                    Histamine Research Society ... [et al.], (2007 Jul) Vol.
                    56, No. 7, pp. 269-73.
                    Journal code: 9508160. ISSN: 1023-3830.
PUB. COUNTRY:       Switzerland
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:         Entered STN: 31 Jul 2007
                    Last Updated on STN: 24 Oct 2007
AB    Gender differences and variations in inflammatory disease (e. g.
      atherosclerosis, neurological disorders, periodontitis and rheumatoid
      arthritis) severity with female sex hormone level have been reported,
      suggesting that female sex hormones modulate the inflammatory response.
      Estrogens act on gene transcription via estrogen receptors alpha and beta.
      Identification of estrogen-regulated genes is a matter of great interest since
      it will contribute significantly to the understanding of the physiological
      importance of estrogens. Anti-inflammatory as well as pro-inflammatory
      responses to estrogens have been reported.  Data have been presented showing
      that estrogens down-regulate the expression of adhesion and chemokine
      molecules in response to inflammation promoters in various experimental
      systems. Functional data show that estrogen treatment attenuates recruitment
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and adhesion of leukocytes to the endothelium induced by inflammation promoters offering a possible mechanism by which estrogens exert an anti-inflammatory effect. These effects of estrogens, with focus on the interactions of monocytes with the vascular endothelium, are highlighted in this review.

L33 ANSWER 2 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2007406868 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17624942
TITLE: Convergence of immunoreceptor and integrin signaling.
AUTHOR: Abram Clare L; Lowell Clifford A
CORPORATE SOURCE: Department of Laboratory Medicine, University of California, San Francisco, CA 94143-0451, USA.
CONTRACT NUMBER: AI065495 (NIAID)
AI068150 (NIAID)
T32 CA009043 (NCI)
SOURCE: Immunological reviews, (2007 Aug) Vol. 218, pp. 29-44.
Ref: 122
Journal code: 7702118. ISSN: 0105-2896.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200709
ENTRY DATE: Entered STN: 13 Jul 2007
Last Updated on STN: 8 Sep 2007
Entered Medline: 7 Sep 2007

AB A common signaling pathway is known to operate downstream of immunoreceptors, such as the T-cell, B-cell, or Fc receptors, following engagement by their respective ligands. This pathway involves Src family kinase-mediated tyrosine phosphorylation of immunoreceptor tyrosine-based activation motifs (ITAMs) that recruit and activate spleen tyrosine kinase (Syk) or Zap70 (zeta-associated protein of 70 kDa) kinases, which in turn activate a variety of downstream signals. Evidence has been building from a variety of sources, particularly mouse models, that molecules involved in the immunoreceptor signaling pathway are also required for signals initiated by integrins. Integrins are the major cell surface receptors that mediate adhesion of leukocytes to a variety of extracellular matrix proteins and counter-receptors expressed on endothelial cells. Integrin ligation is a critical step in the activation of leukocyte effector functions (such as neutrophil degranulation or lymphocyte proliferation). Integrin signaling through pathways common to those utilized by immunoreceptors provides a mechanism by which leukocyte adhesion can regulate activation of cellular responses. In animal models, integrin-mediated signal transduction plays a critical role in inflammatory disease. In this review, we discuss the convergence of immunoreceptor and integrin signaling, focusing on how these pathways modulate leukocyte activation.

L33 ANSWER 3 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2007401530 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17562818
TITLE: Tissue factor: a mediator of inflammatory cell recruitment, tissue injury, and thrombus formation in experimental colitis.
AUTHOR: Anthoni Christoph; Russell Janice; Wood Katherine C; Stokes Karen Y; Vowinkel Thorsten; Kirchhofer Daniel; Granger D

Neil
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, Louisiana State University Health Sciences Center, Shreveport, LA 71130, USA.
CONTRACT NUMBER: R01 DK 65649 (NIDDK)
SOURCE: The Journal of experimental medicine, (2007 Jul 9) Vol. 204, No. 7, pp. 1595-601. Electronic Publication: 2007-06-11.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200709
ENTRY DATE: Entered STN: 11 Jul 2007
Last Updated on STN: 18 Sep 2007
Entered Medline: 17 Sep 2007
AB There is growing evidence for an interplay between inflammatory and coagulation pathways in acute and chronic inflammatory diseases. However, it remains unclear whether components of the coagulation pathway, such as tissue factor (TF), contribute to intestinal inflammation, and whether targeting TF will blunt the inflammatory cell recruitment, tissue injury, and enhanced thrombus formation that occur in experimental colitis. Mice were fed 3% dextran sodium sulfate (DSS) to induce colonic inflammation, with some mice receiving a mouse TF-blocking antibody (muTF-Ab). The adhesion of leukocytes and platelets in colonic venules, light/dye-induced thrombus formation in cremaster muscle microvessels, as well as disease activity index, thrombin-antithrombin (TAT) complexes in plasma, and histopathologic changes in the colonic mucosa were monitored in untreated and muTF-Ab-treated colitic mice. In untreated mice, DSS elicited the recruitment of adherent leukocytes and platelets in colonic venules, caused gross and histologic injury, increased plasma TAT complexes, and enhanced thrombus formation in muscle arterioles. muTF-Ab prevented elevation in TAT complexes, reduced blood cell recruitment and tissue injury, and blunted thrombus formation in DSS colitic mice. These findings implicate TF in intestinal inflammation and support an interaction between inflammation and coagulation in experimental colitis.

L33 ANSWER 4 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2003426140 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12939734
TITLE: Benefits of gliclazide in the atherosclerotic process: decrease in monocyte adhesion to endothelial cells.
AUTHOR: Renier Genevieve; Mamputu Jean-Claude; Serri Omar
CORPORATE SOURCE: CHUM Research Centre, Metabolic Unit, Notre-Dame Hospital, Montreal Quebec, Canada.
SOURCE: Metabolism: clinical and experimental, (2003 Aug) Vol. 52, No. 8 Suppl 1, pp. 13-8. Ref: 47
Journal code: 0375267. ISSN: 0026-0495.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 12 Sep 2003
Last Updated on STN: 1 Oct 2003
Entered Medline: 30 Sep 2003

AB Atherosclerotic cardiovascular disease is the leading cause of premature death in patients with diabetes. Atherosclerosis is a chronic immune-mediated disease, the initiation, progression, and destabilization of which is driven and regulated by inflammatory cells. One critical event in the initiation of this vascular inflammatory disease is the adhesion of leukocytes to the activated endothelium and their migration into the vessel wall. These processes are mediated by the upregulation of adhesion molecules on endothelial cells (ECs) and an increased expression in the vascular wall of chemotactic factors to leukocytes. Monocyte binding to ECs is increased in diabetes. One major determinant of this alteration could be oxidative stress. Given the free-radical scavenging activity of gliclazide, we determined the ex vivo and in vitro effects of this drug on human monocyte binding to ECs and the molecular mechanisms involved in this effect. Our results demonstrate that short-term administration of gliclazide to patients with type 2 diabetes normalizes the levels of plasma lipid peroxides and monocyte adhesion in these subjects. Gliclazide (10 microg/mL) also reduces oxidized low-density lipoprotein (oxLDL)- and advanced glycation end product (AGE)-induced monocyte adhesion to ECs in vitro. The inhibitory effect of this drug on AGE-induced monocyte adhesion involves a reduction in EC adhesion molecule expression and inhibition of nuclear factor kappaB (NF-kappaB) activation. In addition, gliclazide inhibits oxLDL-induced monocyte adhesion to cultured human aortic vascular smooth muscle cells (HASMCs) in vitro and reduces the production of monocyte chemotactic protein-1 (MCP-1) by these cells. Taken collectively, these results show that gliclazide, at concentrations in the therapeutic range, inhibits ex vivo and in vitro monocyte adhesiveness to vascular cells. By doing so, this drug could reduce monocyte recruitment into the vessel wall and thereby contribute to attenuating the sustained inflammatory process that occurs in the atherosclerotic plaque. These findings suggest that treatment of diabetic patients with this drug may prevent or retard the development of vasculopathies associated with diabetes.

L33 ANSWER 5 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2003301513 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12829084
TITLE: Relationship between coagulation cascade, cytokine, adhesion molecule and aortic aneurysm.
AUTHOR: Nomura Fumikazu; Ihara Akihiro; Yoshitatsu Masao; Tamura Kentaro; Katayama Akira; Ihara Katsuhiko
CORPORATE SOURCE: Department of Cardiovascular Surgery, National Hospital Kure Medical Center, 3-1 Aoyama, Kure, 737-0023, Hiroshima, Japan.. fnomura@kure-nh.go.jp
SOURCE: European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery, (2003 Jun) Vol. 23, No. 6, pp. 1034-8; discussion 1038-9.
Journal code: 8804069. ISSN: 1010-7940.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 28 Jun 2003
Last Updated on STN: 3 Sep 2003
Entered Medline: 2 Sep 2003

AB OBJECTIVES: Patients with aortic aneurysm (AA) were in the chronic inflammatory condition and are often combined with disseminated intervascular coagulation. Recent studies demonstrated that atherosclerosis was inflammatory disease. AA and severe atherosclerosis with ulcer formation

contain macrophages and T lymphocytes and accelerate the production of interleukin (IL)-2, which activates lymphocytes and lead to further adhesion of leukocytes. This study was designed to clarify the coagulation condition, cytokine, adhesion molecule, and collagen turnover in patients with AA and finally their relationship with the aneurysmal size. METHODS: Thrombin-antithrombin III complex (TAT), plasma D-dimer, serum type III procollagen peptide (PIIIP), serum soluble IL-2 receptor (sIL-2R), Free tissue factor pathway inhibitor (TFPI), and soluble intercellular adhesion molecule (ICAM-1) were measured preoperatively around the same period when computed tomography (CT) was taken in 17 patients with AA (mean age: 72.2 years). Age-matched (mean age:70 years) volunteers were served as control. Maximum aneurysmal size was measured by CT and aneurysmal volume was also calculated from CT. RESULTS: AA patients showed significantly higher level in preoperative TAT and D-dimer compared to control (TAT: control 2.5+/-1.2 ng/ml, pre 7.2+/-4.5,ng/ml; P=0.0001; D-dimer: control 107+/-46 U/ml, pre 420+/-256 U/ml; P=0.0001). Cytokine also showed higher level preoperatively (sIL-2R: control 398+/-132 U/ml, pre 735+/-260 U/ml; P=0.0001). TFPI showed higher value preoperatively (control 22.9+/-4.9 ng/ml, pre 30.4+/-6.9 ng/ml; P=0.003). PIIIP (collagen turnover) showed no difference between the groups (P=0.0057) and neither did ICAM-1(P=0.0087). TAT (r=0.799, P=0.0001), D-dimer (r=0.56, P=0.0193), sIL-2R (r=0.709, P=0.0021), PIIIP (r=0.561, P=0.00239), and sICAM-1 (r=0.505, P=0.046) level showed positive correlation with aortic aneurysmal size and also TAT D-dimer, and sIL-2R levels were positively correlated with aneurysmal volume (r=0.714 P=0.0013, r=0.556 P=0.00204, r=0.693 P=0.0029, respectively). CONCLUSIONS: AA patients were in the hypercoagulation and inflammatory condition. Aneurysmal size was well correlated with TAT, D-dimer, sIL-2R, PIIIP, and sICAM-1, suggesting that these markers could be good diagnostic and monitoring tool for the disease progression.

L33 ANSWER 6 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2003196949 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12716476
TITLE: The isoprostane 8-iso-PGE2 stimulates endothelial cells to bind monocytes via cyclic AMP- and p38 MAP kinase-dependent signaling pathways.
AUTHOR: Huber Joakim; Bochkov Valery N; Binder Bernd R; Leitinger Norbert
CORPORATE SOURCE: Department of Vascular Biology and Thrombosis Research, University of Vienna, Schwarzspanierstrasse 17, A-1090 Vienna, Austria.
SOURCE: Antioxidants & redox signaling, (2003 Apr) Vol. 5, No. 2, pp. 163-9.
Journal code: 100888899. ISSN: 1523-0864.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 29 Apr 2003
Last Updated on STN: 17 Dec 2003
Entered Medline: 12 Dec 2003

AB Increased levels of isoprostanes have been detected in human atherosclerotic lesions. To examine a possible role for 8-iso-prostaglandin E(2) (8-iso-PGE(2)) in atherogenesis, we tested the effect of 8-iso-PGE(2) on adhesion of leukocytes to human umbilical vein endothelial cells (EC). We demonstrate that 8-iso-PGE(2) stimulates EC to bind monocytes, but not neutrophils. This effect was inhibited by the thromboxane A(2) receptor antagonist SQ29548. Moreover, 8-iso-PGE(2) increased levels of cyclic AMP in EC, and monocyte

adhesion induced by 8-iso-PGE(2) was blocked by a protein kinase A inhibitor, H89. In addition, 8-iso-PGE(2)induced phosphorylation of p38 and extracellular signal-regulated kinase (ERK) 1/2 mitogen-activated protein (MAP) kinase and stimulated expression of EGR-1. A specific inhibitor of p38 MAP kinase (SB203580) abrogated monocyte binding, whereas an inhibitor of the ERK pathway (PD98059) did not block monocyte adhesion induced by 8-iso-PGE(2). Activation of nuclear factor-kappaB (NF-kappaB) and expression of NFkappaB-dependent genes intercellular adhesion molecule-1, vascular cell adhesion molecule-1, and E-selectin were not induced by 8-iso-PGE(2). Taken together, these results demonstrate that 8-iso-PGE(2) stimulates EC to specifically bind monocytes, but not neutrophils. This effect is mediated by cyclic AMP/protein kinase A- and p38 MAP kinase-dependent pathways and is independent of the classical inflammatory NFkappaB pathway. Thus, formation of 8-iso-PGE(2) may play an important role in chronic inflammatory diseases such as atherosclerosis by increasing adhesion and extravasation of monocytes.

L33 ANSWER 7 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2003116754 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12630524
TITLE: Protective effect of 3-deazaadenosine in a rat model of lipopolysaccharide-induced myocardial dysfunction.
AUTHOR: Braun-Dullaeus Ruediger C; Dietrich Simon; Schoaff Michael J; Sedding Daniel G; Leithaeuser Boris; Walker Gerhard; Seay Ulrike; Matthias Reinhard F; Kummer Wolfgang; Tillmanns Harald; Haberbosch Werner
CORPORATE SOURCE: Department of Internal Medicine/Cardiology, Giessen University, Giessen, Germany.
SOURCE: Shock (Augusta, Ga.), (2003 Mar) Vol. 19, No. 3, pp. 245-51.
Journal code: 9421564. ISSN: 1073-2322.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 13 Mar 2003
Last Updated on STN: 16 Oct 2003
Entered Medline: 15 Oct 2003

AB Severe sepsis is accompanied by a profound depression of myocardial contractility. Leukocyte adhesion with subsequent local excess nitric oxide and reactive oxygen species production play major roles for this deleterious effect. We hypothesized that 3-deazaadenosine (c3Ado), an adenosine analogue with anti-inflammatory properties, prevents endotoxin-induced myocardial dysfunction. Wistar rats (8 per group) were treated with Escherichia coli lipopoly-saccharide (LPS, 1 mg/kg, i.p., strain 0111:B4) +/- c3Ado (10 mg/kg, i.p.) 8 h before their hearts were harvested for isolated perfusion, histochemical analysis, or electrophoretic mobility shift assay. LPS induced a marked depression of left ventricular contractility. Immunohistochemistry revealed an upregulation of the adhesion molecules VCAM-1, ICAM-1, and P-selectin within the postcapillary venules. c3Ado inhibited VCAM-1 and ICAM-1 upregulation, but not P-selectin, and prevented cardiodepression. Electrophoretic mobility shift assay revealed inactivation of the transcription factor nuclear factor-kappaB and immunohistochemical staining for gp91phox, ED1, and CD11b demonstrated that c3Ado prevented local recruitment of monocytes and polymorph nuclear neutrophils to the myocardium. Accordingly, significantly fewer leukocytes producing nitric oxide or reactive oxygen species accumulated within the myocardium. Intravital microscopy of intestinal venules confirmed that LPS-induced adhesion of leukocytes was

prevented by c3Ado. Additionally, c3Ado prevented LPS-induced elevation of serum tumor necrosis factor-alpha levels. Our results imply that c3Ado may prove to have clinical relevance for inflammatory disease processes.

L33 ANSWER 8 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2003020982 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12527821
TITLE: [N acetyl-aspartyl glutamic acid (NAAGA) inhibits the adhesion of leukocytes to activated endothelial cells and down-modulates the cytokine-induced expression of adhesion molecules]. Effets inhibiteurs du dipeptide N-acetyl-aspartyl-glutamate (NAAGA) sur l'adherence des leucocytes humains aux cellules endotheliales activees et l'expression des molecules d'adhesion CD11b, CD49d, ICAM-1, ICAM-2, VCAM-1 et ELAM-1.
AUTHOR: Bouhlal H; Blondin C; Haeffner-Cavaillon N; Goldschmidt P
CORPORATE SOURCE: Hopital Broussais, INSERM U430, 96, rue Didot, 75014 Paris.
SOURCE: Journal francais d'ophtalmologie, (2002 Dec) Vol. 25, No. 10, pp. 993-1000.
Journal code: 7804128. ISSN: 0181-5512.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 16 Jan 2003
Last Updated on STN: 28 Aug 2003
Entered Medline: 27 Aug 2003

AB BACKGROUND: Cell adhesion plays a pivotal role in most ocular surface inflammatory diseases. Adhesion molecules mediate cell-to-cell and cell-to-matrix adhesion. Their expression is up-regulated by pro-inflammatory stimuli such as cytokines, histamine or complement-derived anaphylatoxins. The dipeptide N acetyl-aspartyl glutamic acid (NAAGA) is used as unpreserved topical eyedrops in the treatment of allergic conjunctivitis. NAAGA is known to inhibit leukotriene synthesis, histamine release by mast cells, and complement-derived anaphylatoxin production. PURPOSE: To investigate the potential capability of NAAGA to interfere with leukocyte adhesion to endothelial cells and modulate cytokine-induced expression of adhesion molecules. METHODS: Human blood-derived leukocytes were co-cultured with human umbilical vein endothelial cells (HUVECs) in the absence or the presence of 1000 UI/mL human recombinant TNFalpha, 10(-4) M histamine di-hydrochloride or 5x10(-6) M human recombinant C5a, and in the absence or presence of NAAGA (final concentration 2.45%). Adhesion of leukocytes to HUVECs was calculated by subtracting the number of nonadherent leukocytes from the total number of leukocytes. Expression of adhesion molecules was assessed by flow cytometry using anti-CD11b, anti-CD49d, anti-ICAM-1 (CD54), anti-ICAM-2 (CD102), anti-VCAM-1 (CD106) and anti-ELAM-1 (CD62E) monoclonal antibodies. RESULTS: NAAGA was found to totally inhibit adhesion of unstimulated leukocytes, or leukocytes activated with C5a, TNFalpha, or histamine, to TNFalpha-stimulated HUVECs (P=0.0001). Adhesion of leukocytes to unstimulated HUVECs was not modified by NAAGA. Similar results were obtained with endothelial cells stimulated by histamine or C5a. Taken together, these data indicate that NAAGA totally abrogates cell adhesion under inflammatory conditions, without interfering with the physiological adhesion of leukocytes to normal endothelium. At the molecular level, NAAGA inhibited histamine-induced expression of CD11b (P=0.0004) and CD49d (P=0.0045) on granulocytes. On TNFalpha-activated HUVECs, NAAGA induced a significant decrease in the VCAM-1

expression level (P<0.0001) and totally reversed TNFalpha-induced overexpression of ICAM-1 (P=0.0069), ICAM-2 and ELAM-1 (P<0.0001), without interfering with baseline expression of these molecules. CONCLUSION: These results show that the antiallergic compound NAAGA directly inhibits leukocyte adhesion to endothelial cells induced by pro-inflammatory stimuli, and abrogates TNFalpha-induced expression of adhesion molecules on granulocytes and endothelial cells. This capacity to block overexpression of selectins and integrins induced by pro-inflammatory stimuli confers to NAAGA a potential as an anti-inflammatory drug, since interfering with adhesion molecule expression is probably one of the most efficient ways to curb leukocyte recruitment to inflammatory sites.

L33 ANSWER 9 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2002194694 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11927653
TITLE: T cell-mediated signaling to vascular endothelium: induction of cytokines, chemokines, and tissue factor.
AUTHOR: Monaco Claudia; Andreakos Evangelos; Young Sylvia; Feldmann Marc; Paleolog Ewa
CORPORATE SOURCE: Kennedy Institute of Rheumatology Division, Faculty of Medicine, Imperial College of Science, Technology & Medicine, London, United Kingdom.. c.monaco@ic.ac.uk
SOURCE: Journal of leukocyte biology, (2002 Apr) Vol. 71, No. 4, pp. 659-68.
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 4 Apr 2002
Last Updated on STN: 3 May 2002
Entered Medline: 2 May 2002
AB Adhesion of leukocytes to the vascular endothelium is an early event in inflammation. Since cell-cell signaling may be an important stimulus for endothelial activation, we focused in this study on the role of contact-mediated activation by T lymphocytes of endothelial cells (EC). T lymphocytes were cultured with anti-CD3 monoclonal antibody or in the presence of a combination of TNF-alpha, interleukin (IL)-6, and IL-2, prior to fixation and coculture with human umbilical vein EC. Fixed, activated (anti-CD3- or cytokine-stimulated), but not unstimulated T cells, induced release of monocyte chemotactic protein-1, IL-8, and IL-6 by EC in a contact-dependent manner. Moreover, expression of tissue-factor antigen and activity was also significantly increased. Addition of anti-CD40 ligand antibody abolished T cell-induced activation of EC. Our data suggest that contact-mediated activation of EC by T cells, involving ligand:counter ligand interactions such as CD40:CD40 ligand, may represent a novel pathogenic mechanism of progression in inflammatory diseases such as atherosclerosis or rheumatoid arthritis.

L33 ANSWER 10 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2002161299 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11892934
TITLE: Endothelium as a pharmacological target.
AUTHOR: d'Alessio P
CORPORATE SOURCE: Department of Cell Biology, CHU-Necker Enfants Malades, University Rene Descartes Paris V, France.. dalessio@necker.fr

SOURCE: Current opinion in investigational drugs (London, England : 2000), (2001 Dec) Vol. 2, No. 12, pp. 1720-4. Ref: 60
Journal code: 100965718. ISSN: 1472-4472.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 15 Mar 2002
Last Updated on STN: 30 Aug 2002
Entered Medline: 29 Aug 2002

AB Over the last few years, the increasing knowledge of the endothelium has highlighted its integral role in a number of pathologies. Endothelial cells are pivotally involved in the recruitment and adhesion of leukocytes and platelets, and they express adhesion molecules and growth factors. This review highlights the recent advances made in the understanding of the endothelium and discusses the endothelium as a potential target in a variety of diseases, including cardiovascular diseases, cancer and inflammatory diseases.

L33 ANSWER 11 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2001464322 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11509334
TITLE: Interferon-gamma stimulates fractalkine expression in human bronchial epithelial cells and regulates mononuclear cell adherence.
AUTHOR: Fujimoto K; Imaizumi T; Yoshida H; Takanashi S; Okumura K; Satoh K
CORPORATE SOURCE: Department of Vascular Biology, Institute of Brain Science, Hirosaki University School of Medicine, Hirosaki, Japan.
SOURCE: American journal of respiratory cell and molecular biology, (2001 Aug) Vol. 25, No. 2, pp. 233-8.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20 Aug 2001
Last Updated on STN: 15 Oct 2001
Entered Medline: 11 Oct 2001

AB Bronchial epithelial cells may contribute to airway inflammation by releasing chemokines and expressing surface membrane molecules involved in the adhesion of leukocytes. We found that interferon (IFN)-gamma stimulates expression of fractalkine, a potent chemoattractant for monocytes and T lymphocytes, in a time- and concentration-dependent manner by normal human bronchial epithelial cells in culture. Enhanced expression of fractalkine messenger RNA was confirmed by both reverse transcription/polymerase chain reaction and Northern blotting. IFN-gamma also stimulated fractalkine protein production and most of the protein was found in cell lysates. The adherence of blood mononuclear cells to the monolayers of bronchial epithelial cells stimulated with IFN-gamma was partly inhibited by an antifractalkine antibody. An antibody against intercellular adhesion molecule-1 was similarly effective in inhibiting the adhesion. Fractalkine protein levels in bronchoalveolar lavage fluids from patients with inflammatory diseases correlated positively with mononuclear cell counts in the fluids. The bronchial epithelium in a biopsy specimen of lung cancer was stained positively by immunofluorescent staining for fractalkine. We conclude that IFN-gamma stimulates fractalkine expression

by bronchial epithelial cells, which may play an important role in inflammatory responses by recruiting mononuclear leukocytes to the bronchial epithelium.

L33 ANSWER 12 OF 17 MEDLINE on STN
ACCESSION NUMBER: 1998198768 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9539361
TITLE: P-selectin expression in canine cutaneous inflammatory diseases and mast cell tumors.
AUTHOR: Chenier S; Dore M
CORPORATE SOURCE: Departement de pathologie et microbiologie, Faculte de medecine veterinaire, Universite de Montreal, St-Hyacinthe, PQ, Canada.
SOURCE: Veterinary pathology, (1998 Mar) Vol. 35, No. 2, pp. 85-93. Journal code: 0312020. ISSN: 0300-9858.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 11 Jun 1998
Last Updated on STN: 11 Jun 1998
Entered Medline: 4 Jun 1998

AB P-selectin, a member of the selectin family of adhesion molecules, mediates the initial adhesion of leukocytes to the blood vessel wall during their emigration from the circulation. Adhesion molecules play an important role in the pathogenesis of several diseases, including various skin conditions. The objectives of the present study were to characterize the expression of vascular P-selectin in the skin of dogs suffering from inflammatory diseases or from common cutaneous neoplasms, and to determine if a correlation exists between P-selectin expression and inflammatory cell infiltration in these conditions. Immunohistochemistry was performed on formalin-fixed canine skin using a specific anti-canine P-selectin monoclonal antibody (MD3). Results showed that P-selectin was minimally expressed in normal canine skin. However, the number of P-selectin-expressing blood vessels was significantly increased ($P < 0.05$) in cases of allergic dermatitis, autoimmune dermatitis, pyogranulomatous dermatitis, dermatophytosis, and panniculitis. Highest P-selectin expression (percentage of MD3-positive vessels and intensity of the reaction) was observed in cases of autoimmune and pyogranulomatous dermatitis (55.3+/-7.4 and 44.0+/-9.9% P-selectin-positive vessels, respectively). In all conditions studied, a positive correlation existed between the number of P-selectin-positive blood vessels and the number of infiltrating leukocytes ($r=0.556$, $P < 0.01$). A significant number of blood vessels in mast cell tumors also expressed P-selectin, whereas no staining was observed in any of the histiocytomas examined. These results reveal that P-selectin expression is increased in different types of canine inflammatory skin diseases and suggest that P-selectin could participate in the local recruitment of leukocytes in canine cutaneous diseases.

L33 ANSWER 13 OF 17 MEDLINE on STN
ACCESSION NUMBER: 97389373 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9265500
TITLE: Humanization of a mouse antibody against human alpha-4 integrin: a potential therapeutic for the treatment of multiple sclerosis.
AUTHOR: Leger O J; Yednock T A; Tanner L; Horner H C; Hines D K;

Keen S; Saldanha J; Jones S T; Fritz L C; Bendig M M
CORPORATE SOURCE: MRC Collaborative Centre, London, UK.
SOURCE: Human antibodies, (1997) Vol. 8, No. 1, pp. 3-16.
Journal code: 9711270. ISSN: 1093-2607.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X93023; GENBANK-X93024
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 8 Oct 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 22 Sep 1997

AB alpha 4 beta 1 integrin (VLA-4) is crucial for the adhesion of leukocytes to human vascular cell adhesion molecule-1 (VCAM-1) on inflamed endothelium. This cell adhesion event is the first step in leukocyte extravasation across the blood-brain barrier in inflammatory diseases of the central nervous system (CNS) such as experimental autoimmune encephalomyelitis (EAE). Prevention of leukocyte infiltration by antibodies against the alpha 4 integrin, which block the alpha 4 beta 1 integrin/VCAM-1 interaction, have been shown to suppress clinical and pathological features of EAE. In this study, two mouse monoclonal antibodies (MAb) directed against human alpha 4 integrin were analyzed in vitro for their ability to block the interaction of leukocytes with VCAM-1 under different assay conditions. The best blocking MAb, AN100226m, was humanized by complementarily- determining region grafting, associated with human C regions and expressed. We found that modification of two structural determinants (H27 and H29) for the heavy chain CDR1 loop in one hand, and modification of framework amino acid H38, H40 and H44 in the other hand, had no effect on antigen binding. In contrast, modification of a structural determinant (H71) for the heavy chain CDR2 loop resulted in loss of binding. The humanized antibody. AN100226, was equivalent to the murine antibody. AN100226m, in binding to alpha 4 beta 1 integrin and in blocking cell adhesion. More importantly, AN100226 was as effective as AN100226m in the reversal of active EAE in guinea pigs and thus may be useful in the treatment of autoimmune diseases such as multiple sclerosis. AN100226 is currently in phase II clinical trials in the UK for the treatment of multiple sclerosis exacerbations.

L33 ANSWER 14 OF 17 MEDLINE on STN
ACCESSION NUMBER: 96312411 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8701848
TITLE: Alterations in circulating intercellular adhesion molecule-1 and L-selectin: further evidence for chronic inflammation in ischemic heart disease.
AUTHOR: Haught W H; Mansour M; Rothlein R; Kishimoto T K; Mainolfi E A; Hendricks J B; Hendricks C; Mehta J L
CORPORATE SOURCE: Department of Medicine, University of Florida College of Medicine, Gainesville, 32610-0277, USA.
SOURCE: American heart journal, (1996 Jul) Vol. 132, No. 1 Pt 1, pp. 1-8.
Journal code: 0370465. ISSN: 0002-8703.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 12 Sep 1996
Last Updated on STN: 3 Feb 1997

Entered Medline: 3 Sep 1996

AB Atherosclerosis is increasingly thought to be a chronic inflammatory disease. Inflammation requires transmigration of leukocytes from the circulation to the tissues. Adhesion of leukocytes to endothelial calls is the initial event in an inflammatory response and is mediated by expression of several adhesion molecules. In this study we characterize the contribution of intercellular adhesion molecules (ICAM-1) and L-selectin in patients with different coronary artery disease syndromes. Serum concentrations of cICAM-1 and sL-selectin were measured by enzyme-linked immunosorbent assay in 31 patients with stable angina, 30 patients with unstable angina, 18 patients with acute myocardial infarction and 20 healthy subjects in a control group. All patients underwent coronary angiography. Mean (+/-SE) cICAM-1 levels were higher ($p < 0.05$) in patients with stable angina (249 +/- 6 ng/ml), unstable angina (260 +/- 16 ng/ml), or acute myocardial infarction (261 +/- 24 ng/ml) compared with those in subjects in the control group (171 +/- 11 ng/ml). In contrast, levels of sL-selectin were lower ($p < 0.01$) in patients with stable angina (1.2 +/- 0.1 microg/ml), unstable angina (1.1 +/- 0.6 microg/ml), or acute myocardial infarction (1.1 +/- 0.1 microg/ml) compared with those in subjects in the control group (1.8 +/- 0.1 microg/ml). No difference was found in cICAM-1 or sL-selectin levels among patients with stable angina, unstable angina, or acute myocardial infarction. No correlation was seen between cICAM-1 or sL-selectin levels and extent (or severity) of coronary artery disease or leukocyte count. L-selectin expression was observed to be depressed in patients with severe angina compared with that in members of the control group. To examine the mechanism of reduction in sL-selectin levels and L-selectin expression on leukocytes, leukocytes from the control group were stimulated in vitro. Stimulation of leukocytes resulted in a rapid downregulation of surface L-selectin expression, measured by flowcytometry, similar to the suppressed expression of L-selectin found on leukocytes from patients with coronary artery disease. In conclusion, altered cICAM-1 and sL-selectin levels in patients with coronary artery disease reflect the presence of a chronic inflammatory process. This inflammatory process results in downregulation of leukocyte expression of L-selectin and thus lower circulating sL-selectin levels.

L33 ANSWER 15 OF 17 MEDLINE on STN

ACCESSION NUMBER: 95366557 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7543732
TITLE: Flavonoids inhibit cytokine-induced endothelial cell adhesion protein gene expression.
AUTHOR: Gerritsen M E; Carley W W; Ranges G E; Shen C P; Phan S A; Ligon G F; Perry C A
CORPORATE SOURCE: Institute for Bone and Joint Disease and Cancer, Bayer Corporation, West Haven, Connecticut 06516, USA.
SOURCE: The American journal of pathology, (1995 Aug) Vol. 147, No. 2, pp. 278-92.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 21 Sep 1995
Last Updated on STN: 3 Mar 2000
Entered Medline: 12 Sep 1995

AB Treatment of human endothelial cells with cytokines such as interleukin-1, tumor necrosis factor-alpha (TNF-alpha) or interferon-gamma induces the expression of specific leukocyte adhesion molecules on the endothelial cell

surface. Interfering with either leukocyte adhesion or adhesion protein upregulation is an important therapeutic target as evidenced by the potent anti-inflammatory actions of neutralizing antibodies to these ligands in various animal models and in patients. In the present study we report that cotreatment of human endothelial cells with certain hydroxyflavones and flavanols blocks cytokine-induced ICAM-1, VCAM-1, and E-selectin expression on human endothelial cells. One of the most potent flavones, apigenin, exhibited a dose- and time-dependent, reversible effect on adhesion protein expression as well as inhibiting adhesion protein upregulation at the transcriptional level. Apigenin also inhibited IL-1 alpha-induced prostaglandin synthesis and TNF-alpha-induced IL-6 and IL-8 production, suggesting that the hydroxyflavones may act as general inhibitors of cytokine-induced gene expression. Although apigenin did not inhibit TNF-alpha-induced nuclear translocation of NF-kappa B(p50(NFKB1)/p65(RelA)) we found this flavonoid did inhibit TNF-alpha induced beta-galactosidase activity in SW480 cells stably transfected with a beta-galactosidase reporter construct driven by four NF-kappa B elements, suggesting an action on NF-kappa B transcriptional activation. Adhesion of leukocytes to cytokine-treated endothelial cells was blocked in endothelial cells cotreated with apigenin. Finally, apigenin demonstrated potent anti-inflammatory activity in carrageenan induced rat paw edema and delayed type hypersensitivity in the mouse. We conclude that flavonoids offer important therapeutic potential for the treatment of a variety of inflammatory diseases involving an increase in leukocyte adhesion and trafficking.

L33 ANSWER 16 OF 17 MEDLINE on STN
ACCESSION NUMBER: 95160115 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7856732
TITLE: Transforming growth factor-beta 1 null mice. An animal model for inflammatory disorders.
AUTHOR: Kulkarni A B; Ward J M; Yaswen L; Mackall C L; Bauer S R; Huh C G; Gress R E; Karlsson S
CORPORATE SOURCE: Molecular and Medical Genetics Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892.
CONTRACT NUMBER: N0-1-CO-74102 (NCI)
SOURCE: The American journal of pathology, (1995 Jan) Vol. 146, No. 1, pp. 264-75.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 22 Mar 1995
Last Updated on STN: 22 Mar 1995
Entered Medline: 15 Mar 1995

AB Approximately 40% of transforming growth factor-beta 1 null (knockout) mice generated in our laboratory develop normally to term, but 60% die in utero. The animals appear normal during the first 2 weeks of life but develop a rapid wasting syndrome and die by 3 to 4 weeks of age. All of the knockout mice have a multifocal inflammatory disease in many tissues. The heart and lungs are most severely affected. Increased adhesion of leukocytes to the endothelium of pulmonary veins is the initial lesion seen at day 8 postnatally and is soon followed by perivascular cuffing as well as inflammatory infiltrates in lung parenchyma. The lesions in the heart begin as endocarditis and then progress to myocarditis and pericarditis. Within the lung, chronic inflammatory infiltrates consist of T and B lymphocytes,

including plasma cells, whereas macrophages are the primary inflammatory cell type in the heart. Increased expression of major histocompatibility complex class I and II proteins is seen in pulmonary vascular endothelium as early as day 8. An immunoblastic response in mediastinal and mandibular lymph nodes and spleen is also seen. In the absence of any pathogens, this massive inflammatory disease, together with overexpression of major histocompatibility complex class I and II proteins and overproduction of immunoglobulins by lymphocytes, offers circumstantial evidence for an autoimmune etiology.

L33 ANSWER 17 OF 17 MEDLINE on STN
ACCESSION NUMBER: 94110320 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7506711
TITLE: Estradiol enhances leukocyte binding to tumor necrosis factor (TNF)-stimulated endothelial cells via an increase in TNF-induced adhesion molecules E-selectin, intercellular adhesion molecule type 1, and vascular cell adhesion molecule type 1.
AUTHOR: Cid M C; Kleinman H K; Grant D S; Schnaper H W; Fauci A S; Hoffman G S
CORPORATE SOURCE: Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.
CONTRACT NUMBER: DK-08712 (NIDDK)
SOURCE: The Journal of clinical investigation, (1994 Jan) Vol. 93, No. 1, pp. 17-25.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 28 Feb 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 17 Feb 1994

AB Adhesion of leukocytes to endothelial cells is a critical step in the development of acute and chronic inflammatory lesions. We report here that estradiol treatment of cultured human umbilical vein endothelial cells stimulated up to a twofold increase in TNF-induced adhesion of both polymorphonuclear leukocytes and PMA-activated peripheral blood mononuclear cells. This effect was more evident (threefold increase) when endothelial cells were cultured on the basement membrane glycoprotein laminin. Progesterone, but not testosterone, had a similar stimulatory effect. Estradiol also promoted a slight increase in interferon gamma-stimulated endothelial cell adherence for peripheral blood mononuclear cells, but no effect of estradiol was observed when adhesion of leukocytes to endothelial cells was stimulated with IL-1 or IL-4. The estradiol-induced increase in leukocyte binding to human umbilical vein endothelial cells was partially blocked by antibodies to the adhesion molecules E-selectin, intercellular adhesion molecule type 1 (ICAM-1), and vascular cell adhesion molecule type 1 (VCAM-1). Indirect immunofluorescence techniques showed that estradiol produces an increase in TNF-induced cell surface expression of these molecules. Northern blot analysis demonstrated a transient increase in TNF-induced expression of mRNA for E-selectin, ICAM-1, and VCAM-1 in endothelial cells treated with estradiol. Our data demonstrate that estradiol has important regulatory functions in promoting leukocyte-endothelial cell

interactions that might contribute to the observed predominance in females of some autoimmune inflammatory diseases.

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=> s l16 and inflammatory disease
        284191 INFLAMMATORY
           329 INFLAMMATORIES
        284330 INFLAMMATORY
                  (INFLAMMATORY OR INFLAMMATORIES)
       1952243 DISEASE
       1748322 DISEASES
       3226949 DISEASE
                  (DISEASE OR DISEASES)
         21094 INFLAMMATORY DISEASE
                  (INFLAMMATORY(W)DISEASE)
L34   2 L16 AND INFLAMMATORY DISEASE

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L34 ANSWER 1 OF 2   MEDLINE on STN
ACCESSION NUMBER: 2004392733   MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15178558
TITLE: Lysosomal cysteine proteases in atherosclerosis.
AUTHOR: Liu Jian; Sukhova Galina K; Sun Jiu-Song; Xu Wei-Hua; Libby Peter; Shi Guo-Ping
CORPORATE SOURCE: Department of Molecular and Cell Biology, School of Life Science, University of Science and Technology of China, Hefei, Anhui, China.
CONTRACT NUMBER: HL 60942 (NHLBI)
                    HL 67249 (NHLBI)
                    HL-56985 (NHLBI)
                    HL67283 (NHLBI)
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, (2004 Aug) Vol. 24, No. 8, pp. 1359-66. Electronic Publication: 2004-06-03. Ref: 83
                    Journal code: 9505803. E-ISSN: 1524-4636.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
                    General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 7 Aug 2004
                    Last Updated on STN: 11 Feb 2005
                    Entered Medline: 10 Feb 2005
AB Atherosclerosis is an inflammatory disease characterized by extensive remodeling of the extracellular matrix architecture of the arterial wall. Although matrix metalloproteinases and serine proteases participate in these pathologic events, recent data from atherosclerotic patients and animals suggest the participation of lysosomal cysteine proteases in atherogenesis.

Atherosclerotic lesions in humans overexpress the elastolytic and collagenolytic cathepsins S, K, and L but show relatively reduced expression of cystatin C, their endogenous inhibitor, suggesting a shift in the balance between cysteine proteases and their inhibitor that favors remodeling of the vascular wall. Extracts of human atheromatous tissue show greater elastolytic activity in vitro than do those from healthy donors. The cysteinyl protease inhibitor E64d limits this increased elastolysis, indicating involvement of cysteine proteases in elastin degradation during atherogenesis. Furthermore, inflammatory cytokines augment expression and secretion of active cysteine proteases from cultured monocyte-derived macrophages, vascular smooth muscle cells, and endothelial cells and increase degradation of extracellular elastin and collagen. Cathepsin S-deficient cells or those treated with E64d show significantly impaired elastolytic or collagenolytic activity. Additionally, recent in vivo studies of atherosclerosis-prone, LDL receptor-null mice lacking cathepsin S show participation of this enzyme in the initial infiltration of leukocytes, medial elastic lamina degradation, endothelial cell invasion, and neovascularization, illustrating an important role for cysteine proteases in arterial remodeling and atherogenesis.

L34 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2003435064 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 13130482
TITLE: Expression of myeloid-related proteins 8 and 14 in systemic-onset juvenile rheumatoid arthritis.
AUTHOR: Frosch Michael; Vogl Thomas; Seeliger Stephan; Wulffraat Nico; Kuis Wietse; Viemann Dorothee; Foell Dirk; Sorg Clemens; Sunderkotter Cord; Roth Johannes
CORPORATE SOURCE: Institute of Experimental Dermatology and Department of Pediatrics, University of Munster, Munster, Germany.
SOURCE: Arthritis and rheumatism, (2003 Sep) Vol. 48, No. 9, pp. 2622-6.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 18 Sep 2003
Last Updated on STN: 18 Oct 2003
Entered Medline: 17 Oct 2003

AB OBJECTIVE: To analyze which cellular compartments are involved in the initial phase of systemic-onset juvenile rheumatoid arthritis (JRA), and to investigate the role that myeloid-related protein 8 (MRP-8) and MRP-14, two S-100 proteins that are primarily expressed in phagocytes, play in the disease. METHODS: Skin biopsy samples obtained during patients' acute episodes of systemic-onset JRA were analyzed by immunohistochemistry and in situ hybridization. Concentrations of MRP-8/MRP-14 in serum were determined by enzyme-linked immunosorbent assay. RESULTS: By analyzing biopsy samples from cutaneous rashes during the initial phase of systemic-onset JRA, we discovered infiltration of leukocytes expressing MRP-8 and MRP-14. Surprisingly, keratinocytes also showed de novo synthesis of these proinflammatory proteins, indicating activation of epithelial cells during systemic-onset JRA. Serum concentrations of MRP-8/MRP-14 were 120-fold higher compared with healthy controls and approximately 12-fold higher compared with patients with other inflammatory diseases. Concentrations of MRP-8/MRP-14 in patients with systemic-onset JRA fell dramatically after remission was induced. CONCLUSION: The exceptionally high serum levels of MRP-8 and MRP-14 in active systemic-onset JRA make them prime candidates as markers for monitoring disease

activity and response to treatment. Since MRP-8/MRP-14 exhibit direct effects on leukocyte adhesion to the vascular endothelium, their extensive expression in the epidermis indicates an active role for these S-100 proteins in the initial phase of this systemic autoimmune disease.

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FULL ESTIMATED COST	77.92	203.50

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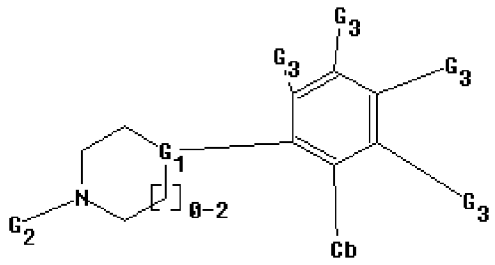

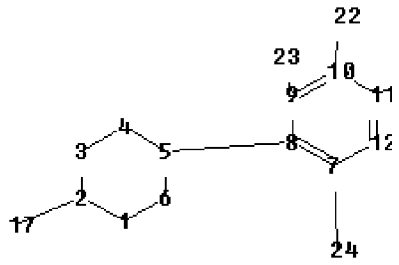

chain nodes :
17 19 20 22 23 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
2-17 5-8 7-24 9-23 10-22 11-20 12-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 2-3 2-17 3-4 4-5 5-6 5-8 7-24 9-23 10-22 11-20 12-19
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 : 7 :

G1:C,N

G2:Cy,Ak,S

G3:X,Cy,Ak,OH,CN,NH2,NO2,H,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 17:CLASS 19:CLASS 20:CLASS 22:CLASS 23:CLASS 24:Atom

L35 STRUCTURE UPLOADED

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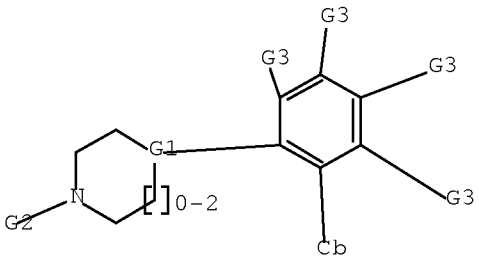
L35 HAS NO ANSWERS
L35 STR



G1 C,N
G2 Cy,Ak,S
G3 X,Cy,Ak,OH,CN,NH2,NO2,H,O

Structure attributes must be viewed using STN Express query preparation.

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4.0% PROCESSED 521732 ITERATIONS 6 ANSWERS

7.2% PROCESSED 923598 ITERATIONS 8 ANSWERS

7.8% PROCESSED 1000000 ITERATIONS 9 ANSWERS
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PROJECTED ITERATIONS: 12885543 TO 12885543
PROJECTED ANSWERS: 83 TO 147

L36 9 SEA SSS FUL L35

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 174.35 377.85

FILE 'CAPLUS' ENTERED AT 17:16:49 ON 13 NOV 2007

FILE COVERS 1907 - 13 Nov 2007 VOL 147 ISS 21
FILE LAST UPDATED: 12 Nov 2007 (20071112/ED)

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L37 3 L36

=> d ibib abs hitstr tot

L37 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:906246 CAPLUS Full-text
DOCUMENT NUMBER: 147:277637
TITLE: Sulfonylated piperidine and piperazine derivatives as 11-βHSD1 inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases
INVENTOR(S): Xiang, Jason Shaoyun; Saiah, Eddine; Tam, Steve Y.; Mckew, John C.; Chen, Lihren; Ipek, Manus; Lee, Katherine; Li, Huan-Qui; Li, Jianchang; Li, Wei; Mansour, Tarek Suhayl; Suri, Vipin; Vargas, Richard; Wu, Yuchuan; Wan, Zhao-Kui; Lee, Jinbo; Binnun, Eva; Wilson, Douglas P.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 277pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007092435	A2	20070816	WO 2007-US3134	20070207
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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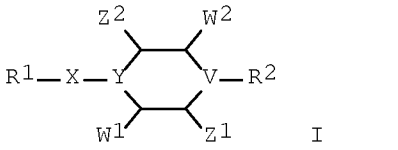
US 2007219198	A1	20070920	US 2007-703522	20070207
PRIORITY APPLN. INFO.:			US 2006-771262P P	20060207
OTHER SOURCE(S):	MARPAT 147:277637			

GI



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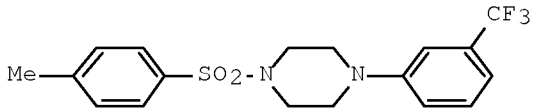


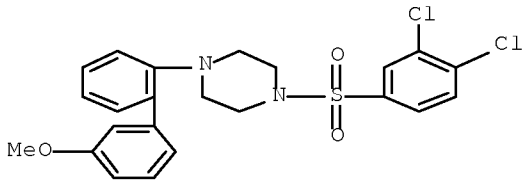
II

AB This invention relates to compds. of formula I that inhibit 11βHSD1. Compds. of formula I wherein R1 is (un)substituted C6-18 (hetero)aryl, (un)substituted C7-20 aralkyl, (un)substituted 6- to 20-membered heteroaralkyl, (un)substituted 8- to 20-membered arylheterocyclyl, (un)substituted 8- to 20-membered aryl(hetero)cycloalkenyl; R2 is (un)substituted C1-18 aryl and (un)substituted 5- to 20-membered heteroaryl; X is SO, SO2, SONH and derivs. and SO2NH and derivs.; V and Y are independently N, CH, C-C1-12 alkyl, provided that Y and V cannot both be CH and C-C1-12 alkyl; W1, Z1, W2 and Z2 are independently C1-12 alkyl, oxo, (un)substituted C6-18 aryl, (un)substituted 5- to 20-membered heteroaryl, C7-20 aralkyl, C3-16 cycloalkyl, 6- to 20-membered heteroaralkyl, etc.; and their pharmaceutically acceptable salts and N-oxides thereof, are claimed. Example compound II was prepared by sulfonylation of 1(3-trifluoromethylphenyl)piperazine with 4-methylbenzenesulfonyl chloride. All the invention compds. were evaluated for their 11-βHSD1 inhibitory activity (no data).

IT 946394-29-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of sulfonylated piperidine and piperazine derivs. as 11-βHSD1 inhibitors useful in the treatment of diseases)

RN 946394-29-2 CAPLUS

CN Piperazine, 1-[(3,4-dichlorophenyl)sulfonyl]-4-(3'-methoxy[1,1'-biphenyl]-2-yl)- (CA INDEX NAME)



L37 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:806254 CAPLUS Full-text
DOCUMENT NUMBER: 147:385945

TITLE: Structure-Activity Relationship Study on N-(1,2,3,4-Tetrahydronaphthalen-1-yl)-4-aryl-1-piperazinehexanamides, a Class of 5-HT7 Receptor Agents. 2

AUTHOR(S): Leopoldo, Marcello; Lacivita, Enza; Contino, Marialessandra; Colabufo, Nicola A.; Berardi, Francesco; Perrone, Roberto

CORPORATE SOURCE: Dipartimento Farmaco-Chimico, Universita degli Studi di Bari, Bari, 70125, Italy

SOURCE: Journal of Medicinal Chemistry (2007), 50(17), 4214-4221
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

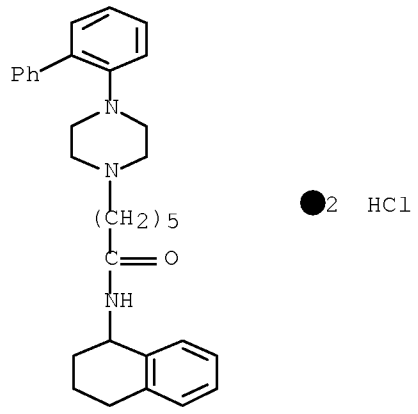
LANGUAGE: English

AB Here the authors report the synthesis of N-(1,2,3,4-tetrahydronaphthalen-1-yl)-4-aryl-1-piperazinehexanamides 16-29 that were designed to elucidate both structure-affinity and -activity relations for the 5-HT7 receptor, by targeting the substituent in 2-position of the aryl linked to the piperazine ring. The affinities of 16-29 for 5-HT7, 5-HT1A, 5-HT2A, and D2 receptors were assessed by radioligand binding assays. The intrinsic activities at the 5-HT7 receptor of the most potent compds. were determined Substituents covering a wide range of electronic, steric, and polar properties were evaluated, revealing a key role on 5-HT7 receptor affinity and intrinsic activity. Certain lipophilic substituents (SCH3, CHMe2, NMe2, CH3, Ph) led to high-affinity agonists, whereas OH and NHCH3 substituents switched intrinsic activity toward antagonism. 4-[2-(1-Methylethyl)phenyl]-N-(1,2,3,4-tetrahydronaphthalen-1-yl)-1- piperazinehexanamide (19), 4-(2-diphenyl)-N-(1,2,3,4-tetrahydronaphthalen- 1-yl)-1-piperazinehexanamide (21), and 4-(2-dimethylaminophenyl)-N- (1,2,3,4-tetrahydronaphthalen-1-yl)-1-piperazinehexanamide (22) were identified as potent 5-HT7 receptor agonists (Ki = 0.13-1.1 nM, EC50 = 0.90-1.77 μM), showing selectivity over 5-HT1A, 5-HT2A, and D2 receptors.

IT 950685-64-0P, 4-(Biphenyl-2-yl)-N-(1,2,3,4-tetrahydronaphthalen-1-yl)-1-piperazinehexanamide dihydrochloride
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity relationship for N-(1,2,3,4-tetrahydronaphthalen-1-yl)-4-aryl-1-piperazinehexanamides as a class of selective 5-HT7 receptor agents)

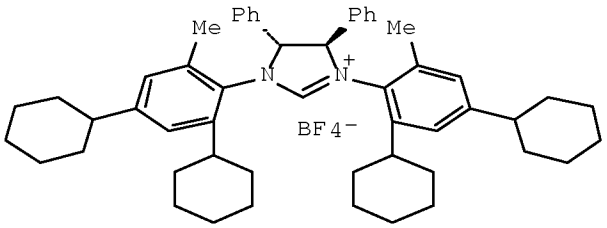
RN 950685-64-0 CAPLUS

CN 1-Piperazinehexanamide, 4-[1,1'-biphenyl]-2-yl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-, hydrochloride (1:2) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:800288 CAPLUS Full-text
DOCUMENT NUMBER: 147:343686
TITLE: New N-Heterocyclic Carbene Ligand and Its Application in Asymmetric Nickel-Catalyzed Aldehyde/Alkyne Reductive Couplings
AUTHOR(S): Chaulagain, Mani Raj; Sormunen, Grant J.; Montgomery, John
CORPORATE SOURCE: Department of Chemistry, University of Michigan, Ann Arbor, MI, 48109-1055, USA
SOURCE: Journal of the American Chemical Society (2007), 129(31), 9568-9569
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

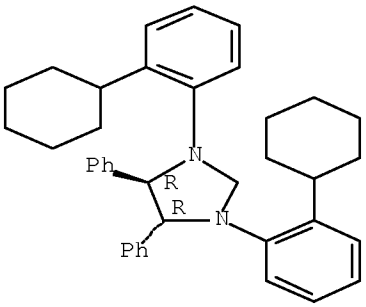
AB A new chiral N-heterocyclic carbene ligand (I) has been prepared and examined in nickel-catalyzed, asym. reductive couplings of aldehydes and alkynes. In comparison with related structures that have been largely examined in asym. ring-closing metathesis reactions, the new ligand provides superior yields and enantioselectivities in the nickel-catalyzed reductive couplings. The scope of asym. couplings in intermol. variants as well as a 14-membered macrocyclization is illustrated.

IT 948892-06-6P 948892-13-5P
RL: CAT (Catalyst use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(preparation of chiral imidazolium ligands via coupling of chiral diamines with aryl or cyclohexyl bromide followed by cyclization for use in asym. coupling reactions)
RN 948892-06-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

CM 1

CRN 948892-05-5
CMF C39 H43 N2

Absolute stereochemistry.



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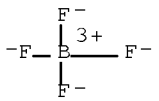
CM 2

CRN 14874-70-5
CMF B F4
CCI CCS



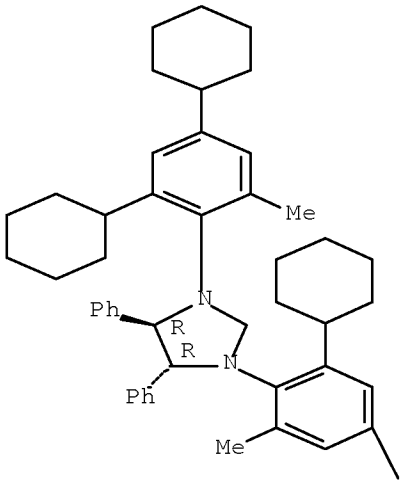
RN 948892-13-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

CM 1

CRN 948892-12-4
CMF C53 H67 N2

Absolute stereochemistry.

PAGE 1-A



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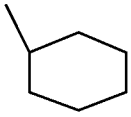

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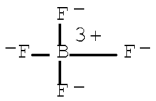


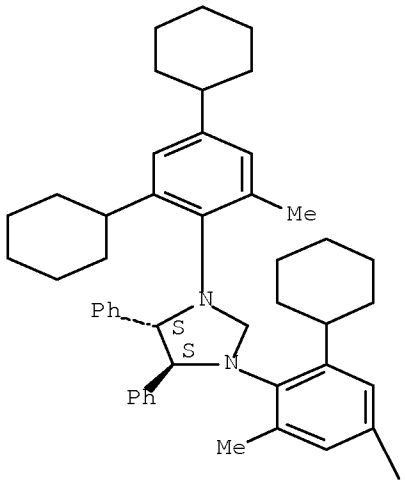
IT 948892-29-3
RL: CAT (Catalyst use); USES (Uses)
(stereoselective preparation of alkenyl silyl ethers via nickel catalyzed coupling of aldehydes with alkynes in the presence of triethylsilane and chiral imidazolium ligands)
RN 948892-29-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

CM 1

CRN 948892-28-2
CMF C53 H67 N2

Absolute stereochemistry.

PAGE 1-A



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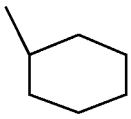

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

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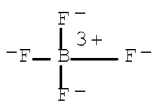
CCI CCS



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L9         48478 S AUTOIMMUNE DISEASE
L10            1 S L9 AND DOPAMINERGIC AGENT

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L18            1 S L16 AND AUTOIMMUNE DISEASE
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L33           17 S L19 AND INFLAMMATORY DISEASE
L34            2 S L16 AND INFLAMMATORY DISEASE

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L37           3 S L36 FULL

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